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# NEURAL CONTROL OF THE PITUITARY GLAND

## I. THE NEUROHYPOPHYSIS*

BY

G. W. HARRIS, M.A., M.D., Sc.D.

*(From the Physiological Laboratory, Cambridge)*

Most endocrine glands either lack a nerve supply or receive only a scanty innervation. The adrenal cortex is believed to be devoid of any nerve supply (Teitelbaum, 1942), whilst the nerve fibres described in the ovary, testis, thyroid, and adenohypophysis (anterior pituitary gland) are probably vasomotor in function. There is no sound evidence that these glands are dependent for their functional activity on a direct secretomotor nerve supply : such dependency seems to be true for only two endocrine glands—the adrenal medulla and neurohypophysis (posterior pituitary gland).

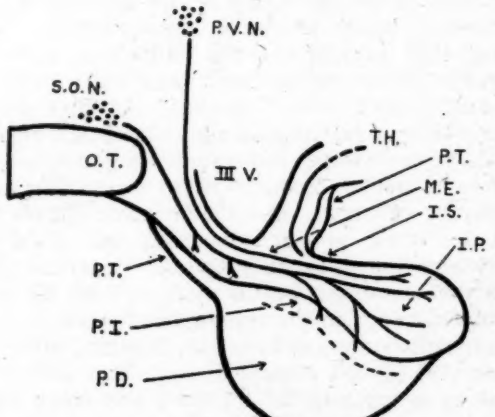
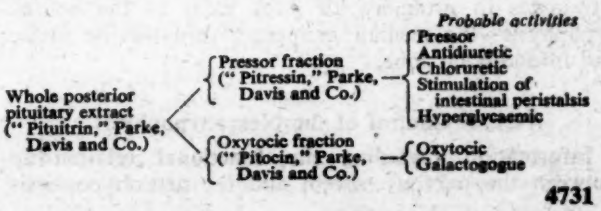



Diagram of a sagittal section through the hypothalamus and pituitary gland. The three parts of the neurohypophysis include the median eminence (M.E.), the constricted infundibular stem (I.S.), and the infundibular process (I.P.). The adenohypophysis also consists of three divisions—the pars distalis (P.D.), the pars intermedia (P.I.), and the pars tuberalis (P.T.). It is established that the neurohypophysis is innervated by the supraoptic nucleus (S.O.N.), situated above the beginning of the optic tract (O.T.), and the paraventricular nucleus (P.V.N.), which is in intimate relationship with the third ventricle (III V.). Other fibres constituting the tubero-hypophysial tract (T.H.) also run to the hypophysis, but their origin is unknown. (By kind permission of the Royal Society of Medicine.)

The terminology adopted in this paper for the different regions of the pituitary gland will be that suggested by Rioch, Wislocki, and O'Leary (1940) (see accompanying illustration). The neurohypophysis is described by these authors as consisting of three subdivisions—the *median eminence* of the tuber cinereum, the *infundibular stem*, and the *infundibular process*. The first two parts may be collectively referred to as the *neural stalk*. This terminology emphasizes the important fact that the upper limit of secreting tissues is in the tuber cinereum. The adenohypophysis is likewise subdivided into three parts—the pars tuberalis, the pars intermedia, and the pars distalis.

### Older Views on the Nature of the Neurohypophysis

Luschka in 1860 recognized the nervous nature of the neurohypophysis and proposed the name " nervendrüse " (nervous gland) for this structure. Peremeschko (1867), who studied the development of the neurohypophysis in various mammals, opposed Luschka's idea that this was a neural structure, and proposed the name " blutgefässdrüse " (blood-vessel gland). For approximately the next 30 years the view was held that the neurohypophysis was neuroglial in nature (see Truscott, 1944). In 1894 Berkley described nerve fibres in the neurohypophysis which he thought were sympathetic in nature, but it was left to Cajal (1894) to describe the important tract of supply to the gland, passing from a nucleus near the optic chiasma through the neural stalk to the infundibular lobe (" superior lobe " of Cajal). On histological grounds Cajal put forward the idea that the neurohypophysis was a sensory organ and that the hypothalamo-hypophysial tract conveyed afferent nerve impulses from the neurohypophysis to the hypothalamus. About this time the pharmacological activity of posterior pituitary (infundibular lobe + pars intermedia) extracts was being studied, and it was found that injection of such extracts had a pressor action (Oliver and Schäfer, 1895; Howell, 1898), a diuretic action in *anaesthetized* animals (Magnus and Schäfer, 1901; Schäfer and Herring, 1906), an antidiuretic and chloruretic action in *unanaesthetized* animals (von den Velden, 1913), a hyperglycaemic action (Borchardt, 1908), a stimulating action on intestinal peristalsis (Bell, 1909), an oxytocic action (Dale, 1909), a galactogogue action (Ott and Scott, 1910), and other effects. In 1928 this single extract with multiple activities was purified and separated into two fractions by Kamm, Aldrich, Grote, Rowe, and Bugbee, working in the research laboratories of Parke, Davis and Co. The names and probable activities of these two fractions are shown below :

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Owing to the fact that the neurohypophysis has little resemblance to a glandular structure, it was at first thought that the active substance present in extracts was formed in the pars intermedia of the adenohypophysis. It was believed that cells, or cellular secretion, passed from the pars intermedia posteriorly into the infundibular lobe, where they were transformed into hyaline masses (Herring bodies) containing the active material. The Herring bodies were thought to migrate up the pituitary stalk and to exert an effect on hypothalamic nerve centres, or to pass into the cerebrospinal fluid of the third ventricle (Cushing, 1932). It can now be stated that (*a*) the active substance present in posterior pituitary extracts is formed in the tissues of the neurohypophysis, though the particular cells involved are unknown; (*b*) that the formation and liberation of any active material by the neurohypophysis is under the direct control of the hypothalamo-hypophysial tract; and (*c*) that any hormone liberated passes into the blood stream; there is no evidence that the pathway is up the stalk to the hypothalamus.

## Nerve Supply of the Neurohypophysis

The original observation of Ramón y Cajal (1894), made on immature mice, that a large number of unmyelinated nerve fibres pass from the hypothalamus to the neurohypophysis, was confirmed by his pupil Tello (1912) on human material. Pines (1925) and Greving (1926) further localized the origin of this tract, as arising largely in the supraoptic and paraventricular nuclei of the hypothalamus, and were responsible for drawing the attention of physiologists and clinicians to this profuse innervation of the neurohypophysis. Fisher, Ingram, Hare, and Ranson (1935) subdivided the hypothalamo-hypophysial tract into two component parts, the supraoptico-hypophysial tract running in the ventral or more rostral wall of the neural stalk and the smaller tubero-hypophysial tract in the dorsal or more caudal wall of this structure. The exact cells of origin of the tubero-hypophysial tract are doubtful. The importance of the supraoptic and paraventricular nuclei in giving rise to the greater number of fibres in the supraoptico-hypophysial tract has been clearly demonstrated by studies of the retrograde degeneration that occurs in these nuclei after lesions placed in the pituitary stalk or tuber cinereum. For example, estimates have been made that in man there are normally about 100,000 nerve fibres present in the supraoptico-hypophysial tract and about 60,000 nerve cells present in each supraoptic nucleus. Following section of the pituitary stalk at the level of the diaphragma sellae in a man 46 years old, only about 9,000 cells were found in each supraoptic nucleus (Rasmussen, 1940). Many data of this type are available also for the rat, dog, and monkey.

The supraoptico-hypophysial tract appears to be the largest, and functionally the most important, innervation of the neurohypophysis. It takes origin largely in the supraoptic and paraventricular nuclei, runs in the ventral wall of the neural stalk (about 10,000 fibres, rat; 60,000, dog and monkey; and 100,000, man) and terminates in probably all three parts of the neurohypophysis—the median eminence, infundibular stem, and infundibular lobe.

## Neural Control of the Neurohypophysis

Information regarding the functional relationship between the nervous system and the neurohypophysis has been arrived at in three main ways. Studies have been made of the effects of (*a*) lesions of the supraoptico-hypophysial tract in patients or experimental animals, (*b*) changing the external or internal environment in such a way that the secretion of the gland is increased (indirect stimulation), and (*c*) direct electrical stimulation of the nerve supply of the gland.

### (a) Lesions of the Supraoptico-hypophysial Tract

Fisher, Ingram, and Ranson (1938) made an important advance in this field, following the rediscovery of the Horsley–Clarke stereotaxic instrument. This is a precision instrument, originally designed and used by Dr. R. H. Clarke and Sir Victor Horsley (1908) for the accurate placement of small lesions in different parts of the cerebellum. By the use of this instrument Ingram *et al.* made localized lesions in different parts of the hypothalamus. They noted in cats that lesions which bilaterally interrupted the supraoptico-hypophysial tract resulted in a condition similar to that of clinical diabetes insipidus. These lesions were situated in the hypothalamus and far enough from the pituitary gland to be sure that no direct damage to the gland or its blood supply had occurred. The normal urine output of a cat is about 100 ml./day, whilst in some of their animals the polyuria, when established, remained in the region of 500 ml./day indefinitely. The urine output of these animals could be brought down to normal levels by replacement therapy with posterior pituitary extracts. Post-mortem examination of the pituitary region revealed that atrophy of the neurohypophysis had occurred; the median eminence and the infundibular stem and process were shrunken and hypercellular, although the pars intermedia and pars distalis appeared normal. In cases of marked diabetes insipidus there was an almost complete absence of nerve fibres in the neurohypophysis. Extracts of these atrophic glands were tested for their pressor, oxytocic, and antidiuretic activity and found to be practically inactive. These results were confirmed on the monkey, both by placing electrolytic lesions in the supraoptico-hypophysial tract in the hypothalamus, and later by Magoun, Fisher, and Ranson (1939), who exposed the pituitary stalk in this animal by a subtemporal approach and made cuts in the median eminence or infundibular stem. Whereas complete transection of the median eminence, or of its anterior half, resulted in a marked polyuria, transection of the infundibular stem (leaving the median eminence part of the neurohypophysis still normally innervated) produced a less severe polyuria, if any at all. These results are enlightening with regard to the results of Mahoney and Sheehan (1936) on the monkey, and Dandy (1940) on the human, who found no, or only mild, polyuria following section of the pituitary stalk. It is probable that in these and other similar cases the tissues of the median eminence were still liberating antidiuretic hormone into the circulation.

The data regarding secretion of the oxytocic substance by the neurohypophysis following interruption of the supraoptico-hypophysial tracts are not so complete as that regarding the antidiuretic hormone. This subject has been reviewed previously (Harris, 1948c), and the position may be summarized by saying that a large proportion of animals in which the supraoptico-hypophysial tracts have been divided have a prolonged labour or deliver their young dead. Similar clinical reports are to be found in the literature (Marañón, 1947). However, a few animals in which the supraoptico-hypophysial

tracts have been interrupted, as shown by a state of diabetes insipidus, have apparently normal labours. The meaning of these results is not clear. It is possible that oxytocic substance is formed elsewhere than the neurohypophysis, or that lack of oxytocic substance may be compensated for by other factors and so result in an apparently normal labour. To test the latter possibility, rats made diabetic by section of the pituitary stalk had either the muscles of the abdominal wall denervated or the nerve supply of the uterus interrupted (Colfer and Harris, unpublished). In some of these animals even these procedures did not prevent normal evacuation of the uterus. (Denervation of the abdominal wall often resulted in the last member of a litter being retained in the vagina, the other members of the litter having been "shunted" into the external world by their next of kin.)

#### (b) Indirect Stimulation

Verney and his colleagues have investigated the mechanism by which the urine flow is affected following changes in the external or internal environment, such as administration of water, exercise, emotional stimuli (noise and pain), and changes in the osmotic pressure of the blood. All these factors appear to exert their effects on the urine volume by changing the rate of secretion of the antidiuretic hormone. The results of many years' work have been reviewed by Verney (1947, 1948), and these papers should be consulted for a detailed discussion and bibliography. It was found that the inhibiting effect of exercise on a water diuresis is due to the emotional accompaniment of that exercise. Dogs submitted to emotional stimuli alone, in the form of loud noises or cutaneous pain, showed similar inhibition of a water diuresis. Many control experiments showed that the antidiuretic response to emotional stress was not mediated by changes in blood pressure or renal blood flow, but was due to a stimulus humorally conducted to the kidney. Dogs in which the posterior pituitary gland had been removed, or in which the supraoptico-hypophysial tracts had been sectioned, showed that these procedures very largely abolished the emotional inhibition of a water diuresis. Thus there is very good evidence that emotional stimuli result in excitation of the supraoptic nuclei, an increased rate of secretion of the antidiuretic hormone, and therefore an inhibition of any concurrent water diuresis. It is of interest that injection of a small dose of adrenaline just before the emotional stimulus prevented the usual antidiuretic response, probably by blocking some neural path leading to the supraoptic nuclei. Adrenaline did not prevent injected posterior pituitary extract from exerting its usual action. In some cases adrenaline liberated from the animal's own gland also appeared to inhibit the release of the antidiuretic hormone following emotional stress. (There are no data on whether adrenaline exerts a similar neural effect in blocking the liberation of the oxytocic substance. This would seem to be of importance in regard to disturbances of parturition and of milk ejection during nursing.)

Many years ago Verney hypothesized that the ingestion of water is followed by a diuresis owing to the fact that the absorbed water lowers the osmotic pressure of the blood and this in turn inhibits the secretion of the antidiuretic hormone by the neurohypophysis. The result is a state of "physiological diabetes insipidus." Direct evidence that changes in the osmotic pressure of the blood do regulate the secretion of the antidiuretic hormone has since been obtained. Short-period injections and long-period infusions of hypertonic sodium chloride solution into the common carotid artery have been shown to cause release of the antidiuretic hormone, with resultant inhibition of a water diuresis. The response was diminished by some 90% after removal of the neural lobe of the pituitary. The osmotic stimulus activates receptive elements situated somewhere in the vascular bed of the internal carotid artery. It is interesting to speculate that the receptive elements may be situated in the supraoptic nucleus, since this structure is so highly vascular and contains small vesicles which Verney has suggested might function as tiny osmometers. A detailed study of the effects of hypertonic solutions enabled Verney to state: ". . . Changes within the range and of the order of 1% in the osmotic pressure of the arterial blood lead, through the intermediation of the antidiuretic hormone, to changes in the rate of water excretion within the range and of the order of 1,000% : the maintenance of near constancy in the osmotic pressure of the internal environment is thereby achieved."

At least some of the fibres which synapse with the cells of the supraoptic nucleus appear to be cholinergic in nature. Pickford (1939) found that intravenous injection of acetylcholine into dogs inhibited a water diuresis, the response being abolished by removal of the neural lobe of the pituitary gland. It was later found that nicotine had a similar action in the human (Burn, Truelove, and Burn, 1945). Pickford (1947) localized the site of action of acetylcholine more exactly by finding that injection of 0.004 ml. (2–4 $\mu$g.) of acetylcholine solution direct into the supraoptic nuclei of dogs resulted in liberation of the antidiuretic hormone. It was then apparent that it was the cells of the supraoptic nucleus, and probably not the cells (if any) upon which the supraoptico-hypophysial tract terminates, that are sensitive to acetylcholine. This is supported by the fact that Feldberg and Vogt (1948) found very low values for the choline acetylase (enzyme system concerned with the formation of acetylcholine) content of the neurohypophysis. Recently Duke, Pickford, and Watt (1950) have been able to produce a reversible state of diabetes insipidus by injection of di-isopropyl fluorophosphate (D.F.P.), an inhibitor of cholinesterase, direct into the supraoptic nuclei of dogs. This procedure resulted in, first, a profound inhibition of urine flow, followed by a polyuria of 4–19 days' duration, and then return of the urine volume to normal values. It would seem, then, that the cells of the supraoptic nucleus are under the control of at least some cholinergic afferent fibres, but that the fibres of the supraoptico-hypophysial tract are not cholinergic in nature.

#### (c) Direct Electrical Stimulation of the Supraoptico-hypophysial Tract

Until a few years ago electrical stimulation of the supraoptico-hypophysial nerve fibres, in order to study the effects of exciting the secretion of the neurohypophysis, was a difficult undertaking. Attempts were made (such as those of Haterius, 1940; Ferguson, 1941; Haterius and Ferguson, 1938), but the fact that anaesthesia itself affects the rate of urine secretion, the level of blood sugar, and so on, made stringent control procedures necessary before any conclusions could be drawn from such experiments. The technical problems were much simplified, however, when it became possible to

stimulate the basal regions of the brain, without anaesthesia, by using the remote control method. In a preliminary operation a small coil was buried between the scalp and skull and an insulated electrode, soldered to one end of this coil, carried down through the skull, corpus callosum, and other midline structures into some part of the hypothalamus or pituitary gland. After recovery from the operation the tissue surrounding the electrode tip could be stimulated by holding a primary coil carrying an alternating current over the animal's head, so that the embedded (secondary) coil was situated in an electromagnetic field. The strength of the stimulus varies inversely as the distance between the two coils, and is thus easily measured and adjusted.

Stimulation of the supraoptico-hypophysial tract by this method has been shown to result in liberation of the antidiuretic hormone and an oxytocic substance, with the following effects on the animal—inhibition of a water diuresis; an increase in the relative, and sometimes absolute, urinary chloride; a marked increase in uterine activity in the oestrous or oestrogenized rabbit, but no increase in the pseudopregnant animal or animal treated with progesterone; an increase in intestinal activity and the appearance of an antidiuretic substance in the urine (Harris, 1947, 1948a, 1948b). Only slight rises in blood pressure were observed after stimulation, but these were of the same type as those following injection of posterior pituitary extract. No hyperglycaemic responses were obtained by stimulating the supraoptico-hypophysial tract or by stimulating different regions of the pituitary gland, though such a response had been claimed by previous workers using anaesthetized animals.

It is of interest that the oestrous rabbit possesses a mechanism (including the supraoptico-hypophysial tract, neurohypophysis, and oxytocic secretion) for increasing the activity of the empty oestrous uterus. Teleologically, there would appear to be no reason for such a mechanism to exist, except the possibility that it might be involved in sperm transport. Parker (1931) found the rate of entry of sperms into the rabbit's uterus too rapid to be accounted for by the rate of swimming of the sperms, and he quotes from an early paper by Heape (1898) in which it was suggested that sperms are drawn into the uterus of the rabbit by a sucking action of the uterus. Heape observed that this uterine activity was induced by stimulating the erectile tissue of the vulva. Krehbiel and Carstens (1939) have confirmed these observations. They found spermatozoa arrive at the utero-tubal junction of rabbits in as short a time as ten minutes after coitus, and, by *x*-ray studies, that various solutions placed in the vagina are carried to the tubal ends of the uterus in two to five minutes if the vulva is artificially stimulated. It seems clear, then, that the ascent of sperm is aided by the motility of the uterus, and that this motility is initiated or increased by vulval stimulation. Since coitus in the rabbit undoubtedly stimulates the adenohypophysis by a nervous reflex, it seems likely that the neurohypophysis may be stimulated by a similar reflex with a resultant oxytocic secretion and increased uterine motility. Since coitus in the rabbit does not result in the release of the antidiuretic hormone (Cross, 1950), then, if the above hypothesis is correct, it would seem that this stimulus causes the release of the oxytocic fraction from the neurohypophysis but not the antidiuretic (pressor) fraction.

In recent years attention has been turned to the relationship between the neurohypophysis and lactation. The process of lactation may be divided into two main phases (Folley, 1947)—first, milk secretion by the cells of the alveolar epithelium, and, secondly, milk discharge or withdrawal from the mammary glands by the suckling young. The first phase of milk secretion is clearly related to the function of the adenohypophysis. It has been suggested by Petersen (see Petersen, 1944) that normal milk discharge is dependent on the neurohypophysis. Petersen suggests that the sensory stimulation of the nipples by the young evokes a nervous reflex in the mother which excites the neurohypophysis to secrete oxytocin. This in turn causes contraction of some muscular element in the breast giving the "let-down" or "draught"—i.e., the milk is positively expressed to the young by the mother. Until recently the evidence in favour of this view was of an indirect nature. Ely and Petersen (1941) showed that after cutting the motor nerves to one half of the udder of cows oxytocin excited, and adrenaline or fright inhibited, the "let-down" in the two halves of the udder alike. Petersen and Ludwick (1942) adduced evidence for the hormonal nature of the stimulus to "let-down" by showing that "let-down" in a perfused udder was excited by adding to the perfusing fluid blood taken from a cow in which "let-down" had been stimulated, but not by adding blood from an unstimulated cow.

A more direct attack on the problem has been undertaken by Cross and Harris (1950) in Cambridge, and Andersson (1951) in Stockholm, the results of these two independent researches being in good accord. Cross and Harris, working on lactating rabbits, found that electrical stimulation of the supraoptico-hypophysial tract under ether anaesthesia resulted in flow of milk up a glass cannula tied into one teat duct. The response was recorded on a kymograph, and was found to have all the characters of one humorally transmitted—long latency, 20–30 seconds, slow rise to peak, and slow subsidence (several minutes). When the stimulation of the supraoptico-hypophysial tract lasted only 15 seconds the response did not start until after the end of stimulation. These responses were similar to those produced by injection of 50–200 mU. oxytocin ("pitocin," Parke, Davis and Co.). Previous cauterization of the supraoptico-hypophysial tract in the median eminence or infundibular stem (Cross and Harris, 1951) abolished this response to stimulation, and also abolished "let-down," so that, despite vigorous suckling on the part of the young, they were unable to obtain more than a fraction of the milk present in the maternal mammary glands. If the mother in which such a lesion had been placed received an injection of oxytocin immediately before suckling, then the milk yield approximated to that obtained before placement of the lesion.

Confirmation of this latter observation has been noted by Harris and Jacobsohn (1951) incidentally in the course of another investigation. Hypophysectomized rats were grafted with anterior pituitary tissue. The grafted tissue was placed under the median eminence in a site where functional activity returns to the graft (this work is described in more detail below). These animals then lacked the greater part of the neurohypophysis but had apparently normal anterior pituitary function. Some of these animals were mated, had normal pregnancies, and delivered living young. In only one out of eight rats that delivered living litters was the litter reared normally. In the other cases milk secretion occurred, but a failure of milk withdrawal resulted in starvation of the vigorously suckling young. It was observed very clearly, however, that if an injection of oxytocin was

made into the mother prompt withdrawal of milk by the young resulted. Repeated injections of oxytocin (three times daily) enabled the litter to be reared. The independent researches of Andersson (1951) were made on sheep and goats using the Hess technique of implanted electrodes to stimulate the hypothalamus in conscious animals. Andersson found that stimulation of some regions in the anterior hypothalamus, in the vicinity of the supraoptic nuclei, induced milk ejection from cannulated teats. The response, recorded by an electrical drop recorder and kymograph, was unaffected by denervation of one half of the udder or by completely anaesthetizing the sacral region of the goat.

It would seem likely, then, that the neurohypophysis is concerned in the process of milk withdrawal by the young. Stimulation of the nipples by suckling appears to excite a reflex nervous release of oxytocin, and so contraction of the myo-epithelial cells (Richardson, 1949) around the mammary alveoli and ducts. It is not yet beyond doubt that oxytocin is alone involved as the humoral stimulus to milk withdrawal. However, if this is so, and the above results are confirmed, then the oxytocic *substance* will have been raised to the status of an oxytocic *hormone*.

It would be of interest to know whether cases of lactational failure in the human, in which the failure is one of disturbed milk withdrawal, would benefit by an injection of oxytocin just before nursing. The work of Newton and Newton (1948) would suggest that this is so. The dose required in the human would probably be in the order of ½ to 1 unit of oxytocin. The results given above throw light on the old clinical observation that breast-feeding aids uterine involution in the post-parturient woman, and would also help to explain the observation of Gunther (1948), who noted an expulsion of milk from the breasts (of a lactating woman) with each labour pain.

### Nature of the Secretion of the Neurohypophysis

A biochemical analysis of the active substance(s) present in an endocrine gland at any one moment throws little light on the way in which these substances are liberated into the blood stream. A major advance in the field of endocrinology will be made when it is found possible to assay the hormone content of venous blood draining particular endocrine glands. In lieu of blood analyses, the most promising approach to the question of what substance(s) an endocrine gland secretes is the observation of the effects of the secretion on the animal itself. In this respect it may be important that there is now available another simple and quick reaction (milk-ejection) by which the secretory activity of the neurohypophysis can be judged. For many years it has been debated whether the neurohypophysis liberates into the blood one hormone with multiple activities or two distinct hormones—one with pressor (and antidiuretic) activity, and the other with oxytocic activity. On the assumption, as seems likely, that it is the oxytocic fraction which is concerned with milk ejection, the following results are of interest with regard to the substance(s) secreted by the neurohypophysis. Cross (1950) has observed that if hydrated rabbits are allowed to suckle their young there is a slight inhibition of a water diuresis, which may be mimicked by injection of 0.5–1 mU. of antidiuretic hormone. Since the oxytocic secretion excited by suckling in the rabbit appears to be of the order of 50–200 mU. there would seem to be a quantitative dissociation between the secretion of the antidiuretic hormone and the oxytocic factor under these conditions. This would indicate the secretion by the neurohypophysis of more than one substance. On the other hand, the observation of Andersson (1951) that intracarotid injection of hypertonic sodium chloride solution, known to cause the liberation of the antidiuretic hormone (Verney, 1947), is effective in producing milk ejection in the goat would tend to link together the secretion of the substances underlying these activities. The conclusions drawn from these results of Cross and of Andersson are discordant, but their work is mentioned here to illustrate the belief that there is now available an important technique by which this problem may be approached.

### Conclusions

Present views with regard to nervous control of the neurohypophysis may be summarized as follows. The glandular tissue of the neurohypophysis, which exists in the infundibular lobe, infundibular stem, and median eminence of the tuber cinereum, is richly innervated by the supraoptico-hypophysial tract of nerve fibres. If this tract is interrupted secretory activity of the neurohypophysis ceases, the gland atrophies, and a state of diabetes insipidus supervenes. In many cases denervation of the neurohypophysis is also followed by dystocia.

Excitation of the gland with release of the antidiuretic hormone follows emotional stress in the normal animal and the intracarotid injection of hypertonic sodium chloride solution; both responses are mediated by the supraoptico-hypophysial tract. Some, at least, of the afferent nervous pathways to the supraoptic nuclei are cholinergic in nature.

Electrical stimulation of the supraoptico-hypophysial tract causes liberation of the antidiuretic and oxytocic substance(s) into the blood, with the following results—inhibition of a water diuresis; increase in the relative, and sometimes absolute, urinary chloride; a marked increase in uterine activity in the oestrous or oestrogenized rabbit, but no increase in the pseudopregnant animal or animal treated with progesterone; an increase in intestinal activity; the appearance of an antidiuretic substance in the urine; and the ejection of milk from the cannulated lactiferous duct of a lactating mammary gland.

It is possible that reflex stimulation of the neurohypophysis follows coitus, and that the resultant increased uterine activity is one factor in the transport of sperm in the female genital tract.

Much evidence now exists that the transfer of milk from a lactating animal to her young is effected by a nervous reflex excitation of the neurohypophysis. The secretion of posterior pituitary hormone causes contraction of some element in the mammary gland and thus a positive ejection of milk from the mother to her suckling young. This milk-ejection response appears to be a function of the oxytocic substance of the neurohypophysis, and the reaction seems to offer a new technique by which the problem of the number of hormones liberated from the neurohypophysis into the blood may be investigated.

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The British European Airways ambulance flight at Renfrew airport (Glasgow) is the subject of a recent article in *John Bull*. It consists of two pilots and two radio-operators, forming two crews who alternate for 24-hour spells of duty. They fly old De Havilland Rapides with a normal cruising speed of 120 m.p.h. to Campbeltown or any of the service airports in the Hebrides, and (in daylight only) to any of 10 emergency landing strips in Highlands, Hebrides, or Orkneys. During 1950 they made 200 trips to carry cases of nephritis, poliomyelitis, fractures, acute appendicitis, and so on, and, since the air ambulance costs at least £16 a flying hour, it is called out only for real need. The aircraft are those used on the regular passenger service: four seats are taken out and replaced by a cradle to hold a stretcher.

# CORTISONE AND A.C.T.H. IN HYPOPITUITARISM


BY

**V. K. SUMMERS, M.D., M.R.C.P.**

*Consultant Physician, Walton Hospital, Liverpool*

AND

**H. L. SHEEHAN, M.D., D.Sc., F.R.C.P., F.R.C.O.G.**

*Professor of Pathology, University of Liverpool*


The isolation of A.C.T.H. has provided a method of replacing the pituitary secretion which influences the adrenal cortex; cortisone provides a method of direct replacement of some of the adrenal cortical hormones. The natural practical application of these two products would therefore be the treatment of adrenal cortical deficiency, either primary, as in Addison's disease, or secondary, as in hypopituitarism. The early discovery that these two hormones have a wide range of other effects led, however, to their being diverted to the treatment of other diseases, and relatively few investigations have been made to assess their value in the treatment of hypopituitarism.

In the literature there are five reports on the treatment of true cases of hypopituitarism with A.C.T.H. The periods of treatment were usually about 6 to 10 days. There was nearly always some clinical improvement during the therapy, but the biochemical effects appear to have been rather variable. Pompen (1950) noted an increase in 17-ketosteroid excretion in the urine and also of oestrogenic substances, but not of corticosteroids. Knowlton *et al.* (1950) observed a slight increase in 17-ketosteroid excretion to 2.6 mg. a day, but no corresponding increase of oestrogen excretion. Bartter *et al.* (1950) treated three patients with A.C.T.H.; all showed a rise in urinary corticosteroid excretion, but only one had an increase of 17-ketosteroid excretion. Seffer, Lestina, and Freeman (1950) observed an increase of 17-ketosteroid excretion.

The nitrogen and electrolyte balance was studied by Bartter *et al.*, who observed some retention of sodium and chlorine, with a loss of nitrogen and calcium and a transient loss of potassium. Knowlton *et al.* also observed the retention of sodium and chlorine, but no alteration in the metabolism of calcium or nitrogen, apart from some increase in the excretion of uric acid.

Schrock, Sheets, and Bean (1951) treated a patient who had a combination of rheumatoid arthritis and hypopituitarism with A.C.T.H. and also with cortisone. Unfortunately this patient was also given testosterone at the same time, so that it is difficult to evaluate the effects of the first two hormones. During the treatment with cortisone signs of myxoedema occurred. The case of "pituitary cachexia" treated with corticotrophic hormone by Hemphill and Reiss (1944) cannot be accepted as a true example of hypopituitarism; there was nothing to suggest that any structural changes had occurred in the pituitary.

## Present Cases

Five patients have been treated in the present study. All were typical cases of hypopituitarism due to postpartum necrosis of the anterior lobe (Sheehan and Summers, 1949). The symptoms and signs were of a severe degree of pituitary deficiency, with permanent

amenorrhoea since the last delivery, complete loss of pubic and axillary hair, and severe atrophy of the thyroid and the uterus. All had a low B.M.R. (between −25% and −50%), low 17-ketosteroid excretion (range from 0 to 1.89 mg. a day, with a mean of 0.62 mg.), and characteristic responses to the insulin-sensitivity test. The duration of the disease varied from 9 to 27 years. Four of the patients had had previous treatment with testosterone, which had produced benefit in three of them but which was completely without effect in the fourth case. This latter patient showed an excellent response to cortisone.

Before beginning therapy the patients were kept in hospital for at least 10 days, so that full clinical and biochemical observations could be made. During this time and during the course of the investigation a varied diet was given, but this was so regulated that the daily intake of sodium, potassium, and chlorine was constant. After the course of cortisone or A.C.T.H. had been completed the patients were left for two weeks without any treatment in order to observe subsequent changes, and testosterone implants were then inserted.

## Cortisone

Three patients were treated with intramuscular injections of 100 mg. of cortisone acetate daily. One patient was treated for 12 days and the other two for 20 days.

### Mental and Physical Changes

Within two days after beginning treatment there was always a very dramatic improvement in the general clinical condition, reaching a maximum at about the third or fourth day and continuing thereafter. Their previous apathy was replaced by an active interest in their surroundings, and they began to read and knit and to help in the ward work. The patients became very loquacious for two or three days, the voice being louder and clearer than before. They were much more alert, and in intelligence tests designed for children of the age of 7 their score, which had previously averaged 50 to 60%, rose to 70 to 80%. The mental improvement continued for about 12 to 15 days, at which time two of the patients became depressed, moody, and very obstinate—so much so that one patient insisted on leaving hospital and the other could be persuaded to remain only by the exercise of much tact. The third patient remained co-operative throughout the treatment.

The patients were physically much more active, and their muscular strength, as measured by a dynamometer, increased slightly: the mean hand-grip before treatment was 18.5 kg.; after 12 days' treatment it was 21 kg.

The cold sensitivity became much less marked, and after about a week all the patients had axillary sweating, which continued for the remainder of the treatment. There was no change in the temperature or in the pulse and respiratory rates. The period of administration of cortisone was too short to produce any recognizable effects on skin pigmentation or on the pubic and axillary hair or eyebrows.

A very interesting effect was noted in one patient who had a gross pyuria, a condition which occurs in a number of patients with hypopituitarism. Within two or three days after starting cortisone the pyuria began to diminish quickly though no other treatment for the urinary infection was given. This improvement continued, so that at 12 days the urine was quite free from pus and remained so. It is also of interest that the partial deafness which was present in two of the patients showed some definite improvement during the administration of the cortisone.

*Blood Pressure and Electrocardiogram.*—The blood pressure showed a rise; the figures before and 11 days after treatment were respectively 105/75 and 140/90, 115/70 and 120/80, and 130/80 and 175/90. Before treatment these patients had characteristic electrocardiographic abnormalities: low-voltage complexes, increase in the P–R interval, and negative T waves in Leads II and III. After about nine days' treatment the tracings were within normal limits.

*Weight and Basal Metabolic Rate.*—Two of the patients gained weight—in one rising from 141 lb. (64 kg.) before treatment to 152 lb. (69 kg.) after 12 days, and in the other rising from 113 to 122 lb. (51.3 to 55.3 kg.) after 19 days' treatment. The weight of the third patient fell from 134 to 132 lb. (60.8 to 59.9 kg.) after 12 days' treatment, but she was deliberately restricting her diet with the object of becoming slim. In all the cases the slight puffiness of the orbital region and the limbs disappeared within a few days. In one patient the B.M.R. rose to −6% after 10 days. In the other two, estimations could not be made after treatment because of the lack of co-operation which developed during treatment.

*Haematology.*—The eosinophil response to the first injection of cortisone was observed in one patient. The eosinophil count fell from 215 to 165 per c.mm. in four hours after the injection. This small fall was well within the normal daily variation in this particular patient. There was a definite improvement in the anaemia in all patients during treatment. The mean haemoglobin rose from 9.6 g. per 100 ml. before treatment to 10.6 g. per 100 ml. after two weeks' treatment; the corresponding red blood counts rose from 3,500,000 to 3,900,000 per c.mm. The eosinophil count showed no change, remaining in the range of 140 to 260 per c.mm.

*Subsequent Clinical Course.*—After the cessation of treatment there was a gradual deterioration in the patients' condition. Nevertheless, even as long as 14 days after the last injection they were definitely a little better than before treatment began. The obstinacy and uncooperativeness gradually lapsed into the passive lethargy of the untreated condition.

### Urine Chemistry

Immediately after the first injection of cortisone there was a pronounced diuresis for a day. The urine output fell at about the third to the sixth day and then increased again, but remained consistently higher than before treatment. Associated with this increased output of urine there was an increased output of urea and uric acid, with a less marked rise in the excretion of creatinine. Glycosuria did not occur. The output of urine, urea, and uric acid continued at above the pre-treatment level for two weeks after treatment had ceased. The mean daily figures were as follows:

| | Urine Vol. (ml.) | Urea (g.) | Uric Acid (g.) | Creatinine (g.) |
|---|---|---|---|---|
| Observation period.. .. | 930 | 10·9 | 0·30 | 0·73 |
| Treatment day 1 .. .. | 2,690 | 12·8 | 0·37 | 0·88 |
| " " 2 .. .. | 1,940 | 21·4 | 0·83 | 1·17 |
| " " 3 .. .. | 1,280 | 24·6 | 0·52 | 0·91 |
| " " 4 to 6 .. | 1,320 | 22·4 | 0·53 | 0·81 |
| " " 7 to 19 .. | 1,740 | 26·8 | 0·60 | 1·01 |
| Subsequent 2 weeks .. | 1,350 | 20·4 | 0·55 | 0·72 |

*17-Ketosteroid Excretion.*—The daily excretion of 17-ketosteroids in the urine was unchanged on the first day of treatment (mean 0.39 mg.), rose slightly on the second day (mean 0.90 mg.), and was relatively high on the third day (mean 2.33 mg.). After this time it continued throughout the period of observation at a mean level of 3.22 mg., ranging from 2.30 to 4.23 mg. a day. After the cortisone was discontinued the 17-ketosteroid excretion in the urine fell gradually, reaching a mean output of 1.88 mg. at four days and 0.46 mg. at seven days. Subsequently the excretion continued at levels similar to those at the time of admission.

*Kepler Tests.*—In all the patients there was a considerably increased diuresis during this test, though in only one was the maximum volume of urine an hour excreted after administration of water greater than the volume of the night urine. The Kepler index, which ranged from 5 to 7 before treatment, rose to 36 to 39 after 10 days' treatment.

#### Blood Chemistry

The blood was examined chemically at weekly intervals during the whole course of the investigation. The levels of sodium, potassium, calcium, chlorine, phosphorus, and cholesterol showed the usual fluctuation from one estimation to the next, but there was no recognizable effect due to the cortisone.

The blood urea tended to rise during the treatment and to remain high during the subsequent two weeks, reaching levels of about 35 to 45 mg. per 100 ml., as compared with the previous range of about 25 to 35 mg. per 100 ml. No significant change occurred in the levels of creatinine or uric acid.

*Insulin-tolerance Tests.*—After cortisone had been administered for nine days the insulin-tolerance tests showed a slight percentage reduction in the sensitivity to insulin and a slight percentage improvement in the response to hypoglycaemia ; the absolute level of the blood sugar was raised. The tests were carried out with 0.03 unit of insulin per kg. of body weight. The following are the mean figures given in mg. of sugar per 100 ml. of blood:

| Minutes after insulin .. | 0 | 20 | 30 | 60 | 90 | 120 |
|---|---|---|---|---|---|---|
| Before treatment .. | 74 | 41 | 39 | 50 | 58 | 61 |
| After 9 days' cortisone .. | 91 | 58 | 55 | 70 | 72 | 82 |

#### Comment

The great improvement in the psychological and physical condition was not paralleled by a corresponding degree of improvement in intellectual and muscular power. There was, however, objective evidence of other improvement, involving many aspects of the hypopituitarism.

The clearing up of gross pyuria in one of the cases is presumably an example of endocrine influence on the urinary tract, opposite in type to that which is manifested in pyelitis of pregnancy.

It is difficult to explain the considerable increase in the excretion of 17-ketosteroids, as in the normal patient cortisone reduces the excretion of these substances. The possibility that some of the breakdown products of the cortisone may have been excreted as 17-ketosteroids cannot be excluded. Nevertheless other aspects of adrenal cortical function, such as those measured by the Kepler and insulin-tolerance tests, show some improvement.

The increase in the basal metabolic rate is a normal finding in any patient treated with cortisone. This may be related to an increase of protein metabolism, as is suggested by the very high output of urea in the urine. It is of interest that the puffiness of the face disappeared at about the same time.

The improvement in the anaemia, though not very great in the course of this short treatment, occurred in all the patients, and is of importance because this type of anaemia is extremely refractory.

In the present series grave difficulties were encountered owing to the psychological disturbances which developed after about two weeks. It is possible that these disturbances may have resulted from too high a dosage. Cook *et al.* (1951) say that one of their patients is doing well on 25 mg. of cortisone daily, given either by tablet or parenterally. Nevertheless there is no doubt that cortisone is the most efficient method of producing clinical improvement in hypopituitarism that has been found up to the present. It gives more rapid results than testosterone, and produces a number of effects which cannot be obtained with that hormone. When cortisone becomes more readily available it should certainly be tested for the long-term maintenance of these patients. No opinion can yet be expressed on its possible value in the treatment of the attacks of coma which may occur in hypopituitarism.

### Adrenocorticotrophic Hormone

Two patients were treated with intramuscular injections of 25 mg. of A.C.T.H. eight-hourly. One patient (Case A) was treated for seven days and the other (Case B) for 15 days.

#### Mental and Physical Changes

This aspect will be considered in two sections: first, the general effect of the treatment; and, secondly, the undesirable side-effects.

No significant change was observed until about the third day, when there was slight flushing of the face, recognizable both by the patient and by the observer. Subsequently there was a gradual but in no way dramatic improvement in the general condition, with an increase in physical strength and the development of a cheerful alertness. The intelligence tests showed no significant improvement. At the same time there was development of slight axillary perspiration, and the sensitivity to cold was less marked. The appetite was rather better. The slightly puffy appearance of the face was unchanged. The blood pressure gradually increased in one patient from 100/75 up to 150/90. The weight remained unchanged.

No change in the B.M.R. was observed after treating Case B for 15 days.

#### Complications of Treatment

The treatment in both these patients had to be stopped, in one case after seven days and in the other after 15 days, because of the development of migraine and hemiparesis, presumably due to a cerebrovascular disturbance. Neither patient had ever suffered from this type of headache before. The first symptom in one case appeared on the sixth day of treatment, when the grip of the left hand, as measured by dynamometer, fell to one-third of that on the other side. The next day she developed a severe headache on the left side, with a typical migraine fortification spectrum, and the weakness of the left hand was more pronounced. About six hours later she suddenly became comatose, with stertorous breathing and

cyanosis. The limbs were flaccid and there was a bilateral extensor plantar reflex; the deep reflexes were diminished for the first half-hour and subsequently became brisk. The pupils were contracted. During the period of unconsciousness, which lasted about five hours, the blood pressure and pulse rate were normal. After this attack the injections of A.C.T.H. were replaced by "dummy" injections of saline at eight-hour intervals. The left arm showed no sensory disturbances, but its muscular power was very weak for three days and did not return to normal until a week after cessation of treatment. The headache on the left side continued with diminishing severity for a further ten weeks.

The other patient complained, from the third day onwards, of headache on the left side and a sensation of flushing of the left side of the face. These symptoms gradually became more severe, and by the twelfth day dynamometer tests showed that the left-hand grip was becoming weak. As this was more marked by the fifteenth day it was considered prudent to stop treatment though no further symptoms had developed. The occurrence of these complications interfered seriously with the planned investigations.

### Haematology

The eosinophil response to the first injection of A.C.T.H. was slight—a fall in four hours from 260 to 190 per c.mm. in Case A, and from 240 to 220 in Case B. These falls are considerably less than the normal response to A.C.T.H. No recognizable improvement occurred in the red count or other haematological findings.

### Urine Chemistry

In both patients there was some diuresis on the first day, more marked in Case A than in Case B. Subsequently the urine volume remained consistently high, and at the same time the output of urea was definitely increased. The excretion of uric acid and of creatinine increased slightly in both cases. The increased output of urine and urea continued, though in less degree, for two weeks after the cessation of treatment. The mean daily outputs were as follows (those for 7 to 15 days are taken from only a single case):

| | Urine Vol. (ml.) | Urea (g.) | Uric Acid (g.) | Creatinine (g.) |
|---|---|---|---|---|
| Observation period | 760 | 9·2 | 0·25 | 0·59 |
| Treatment day 1 | 1,680 | 13·4 | 0·41 | 0·73 |
| ,, ,, 2 | 840 | 8·8 | 0·28 | 0·48 |
| ,, ,, 3 | 1,480 | 12·4 | 0·33 | 0·69 |
| ,, ,, 4 to 6 | 1,080 | 14·8 | 0·32 | 0·63 |
| ,, ,, 7 to 15 | 710 | 16·7 | 0·27 | 0·51 |
| Subsequent 2 weeks | 970 | 14·1 | 0·33 | 0·73 |

*17-Ketosteroid Excretion.*—The urinary 17-ketosteroid excretion on admission was low in Case B (mean 0.37 mg. a day; range 0.20 to 0.63 mg.), but relatively high in Case A (mean 1.08 mg. a day; range 0.96 to 1.20 mg.). The former showed only a gradual rise to a mean of 1.32 mg. a day during the second week. After treatment was stopped her excretion fell within three days to the previous level. The second patient showed a gradual rise during the first three days, and had a mean output of 4.86 mg. a day from the fourth to the seventh day. After the injections were stopped her excretion gradually fell to pre-treatment levels by about the ninth day.

Kepler tests could not be repeated in these patients after treatment.

### Blood Chemistry

Estimations were made at weekly intervals during the whole course of the investigation. There was a slight fall in cholesterol, but this returned to its previous level of 220 to 235 mg. per 100 ml. within a week after cessation of the treatment. No significant change could be detected in the levels of sodium, potassium, calcium, chlorine, or phosphorus, nor in the levels of urea, creatinine, or uric acid.

*Insulin-tolerance Tests.*—It was possible to repeat the insulin-tolerance test in only Case B after treatment. There was a slightly improved response to the hypoglycaemia which followed the administration of insulin. The following are the results of the test carried out with 0.30 unit of insulin per kg. of body weight (the figures are given in mg. of sugar per 100 ml. of blood):

| Minutes after insulin | 0 | 20 | 40 | 60 | 90 | 120 |
|---|---|---|---|---|---|---|
| Before treatment | 70 | 47 | 35 | 35 | 35 | 35 |
| After 15 days' A.C.T.H. | 65 | 30 | 30 | 40 | 55 | 57 |

### Comment

It is only to be expected that, in a patient with a severely atrophied adrenal cortex, some time would elapse before anatomical hypertrophy would permit sufficient increase of function to cause significant clinical effects. In the present study, Case B, who appeared to have the more severe adrenal atrophy as judged by her previous low excretion of 17-ketosteroids, showed the lesser increase of this excretion under treatment and the lesser diuresis. In the short period of therapy the clinical improvement was relatively poor, though it is possible that a greater improvement would be obtained by a more prolonged course of treatment. On the other hand, the peculiar type of migraine attacks were very alarming, and at present it does not seem justifiable to undertake anything except carefully supervised experimental treatment with A.C.T.H. in patients with hypopituitarism.

There appear to be two main types of undesired side-effects following A.C.T.H.: (*a*) those which occur during the administration of the hormone, and (*b*) those which follow its withdrawal.

(*a*) During the administration of the hormone there may be neurological symptoms which seem sometimes to be related to disturbances in the cerebral cortex and meninges, as in the present two cases. Soffer, Levitt, and Baehr (1950) observed convulsions in four patients with disseminated lupus erythematosus who were under this treatment. Dorfman *et al.* (1951) gave A.C.T.H. to children with various diseases; four of them developed status epilepticus followed by coma of varying duration and by transient or permanent neurological abnormalities. Knowlton *et al.* (1950) treated a case of hypopituitarism with various dosages of A.C.T.H. and had finally to terminate the study because the patient had severe abdominal cramps and anoxia. Other recognized complications of A.C.T.H. therapy are more typical results of the stimulation of the adrenal cortex, such as hypertension, episodes of heart failure, and hyperglycaemia.

(*b*) After the A.C.T.H. has been discontinued for a few days there may be evidence of a transient deficiency of adrenal cortical function. Frenkel, Groen, and Hellinga (1950) observed sudden bilateral arthralgia of the knees, a condition which is relatively common in patients with untreated hypopituitarism. Pompen (1950) treated a case of hypopituitarism for six days with

A.C.T.H. A week later she had a sudden collapse with very weak pulse and some oedema of the legs; her blood sugar varied between 40 and 60 mg. per 100 ml., and her serum potassium was 32 mg. per 100 ml.


### Summary

Three patients with hypopituitarism were treated with cortisone for 12 to 20 days. There was a pronounced clinical and biochemical improvement, though a peculiar psychological change occurred after about two weeks. This treatment seems to hold out much promise for the future.

Two patients with hypopituitarism were treated with A.C.T.H.—one for 7 days, the other for 15 days. There was a slight clinical and biochemical improvement, but after a few days both patients developed migraine and hemiparesis, and one became comatose. It sems advisable that A.C.T.H. should be employed only with the greatest caution in the treatment of hypopituitarism.


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During 1949 Unesco organized an experiment in West China to prepare a wide range of visual aids for use in fundamental education (*The Healthy Village*, Unesco, Paris). Dr. Clara Nutting writes about the work of the health department, and describes among other things how health filmstrips were made. The first topic chosen was smallpox. The greatest difficulty lay in explaining to the native artists how to teach the prevention of disease. Next they attacked the problem of trachoma, the cause of 80% of all eye infections in North China, most of which could be avoided if the people were educated to simple health habits. The artists were shown several cases, and followed the treatment; this enabled them to understand the medical side and thus to express their impressions in pictures. Filmstrips on tetanus neonatorum followed, then on safe food and water and on health habits. In the practical field vaccinations were performed in the township of Huang Ke Chen and the rural districts surrounding it; the people co-operated readily. Children under 16 formed 80% of those vaccinated. But there is still need for more education, says the report, as many people never reappear for further vaccination. Filmstrips on trachoma were shown, and all those who reported that they had the disease were registered; market days were chosen for giving examinations and treatment in the town, and the others were devoted to work in the rural districts. Education is still the most essential need, for until the people become trachoma-conscious treatment can never be really effective. Here, as in other diseases, filmstrips and pictures are of great value in teaching preventive medicine.

# EFFECT OF CORTISONE ON CRISIS IN SIMMONDS'S DISEASE


BY

**E. N. ALLOTT, D.M., F.R.C.P.**

AND

**J. H. SIMMONS, M.D., M.R.C.P.**

*(From Lewisham Hospital, London, S.E.13)*


After conversation with Professor Sheehan we decided that it was worth recording these notes on the response of a patient with Simmonds's disease, in crisis, to cortisone.

## Case History

The patient developed Simmonds's disease after her third pregnancy in 1947. Her pregnancy and confinement were normal, but her milk supply stopped after a few weeks and was followed by an amenorrhoea. She then became very tired and lost interest in everything; there was complete loss of libido. On two occasions her 17-ketosteroids were estimated at 1.9 and 2.7 mg. a day. She had been treated with methyl testosterone, 10 mg. thrice daily, thyroid, 1 gr. (65 mg.) daily, and "doca linguets," three daily, with considerable improvement. Her normal blood pressure was 115/75. She was admitted on March 27 for implantation of hormones: the previous therapy was temporarily discontinued.

On admission she was listless but showed no abnormal physical signs. Her blood pressure was 100/60. On March 29 she had nausea and vomited during the night; her temperature went up to 103° F. (39.4° C.); she became very uncooperative and incontinent; and her blood pressure was 84/56. Her condition worsened and she became very drowsy and negativistic and would not answer questions. She lay curled up. Her blood electrolytes at this time were found to be normal: sodium, 137 mEq. per litre; potassium, 4.4 mEq. per litre; chlorine, 100 mEq. per litre; blood urea, 41 mg. per 100 ml. A saline drip was started and treatment with doca, 10 mg. followed by 5 mg. twice daily, was begun. "Eucortone," 15 ml. followed by 10 ml. four-hourly, was also given. Her blood sugar at midnight was found to be 53 mg. per 100 ml. The drip was changed to glucose saline. The blood sugar was still only 41 mg. per 100 ml. at midday on March 30. Her temperature remained high, rising up to 103° F. (39.4° C.). Her condition was otherwise unchanged.

On March 31, although the blood sugar had risen to 107 mg. per 100 ml., her condition was essentially unchanged. Her mental attitude was still childish and she was uncooperative and irritable. Her temperature was still up to 102.5° F. (39.2° C.). Cortisone was therefore started, 100 mg. being given at midday and at 6 p.m. In view of the pyrexia procaine penicillin, 300,000 units twice a day, was also started.

At midday on April 1 the patient's mental condition was much better and by 6 p.m. she was much more rational, though she was still incontinent. The highest temperature during the day was 100.5° F. (38.1° C.). Cortisone, 200 mg., was again given during the day. Next day she was quite reasonable and continence was returning. Cortisone, 100 mg. daily, was continued for a further four days and penicillin was discontinued. On April 3 her temperature was normal and she was well. Her subsequent progress was satisfactory.

Pellets of doca and testosterone were implanted on April 20, since when she has remained well.

### Comment

This patient in severe Simmonds's disease crisis showed very little improvement when treated with eucortone, doca, and glucose saline, even after 48 hours, by which time the blood sugar had returned to normal. Within 24 hours of starting treatment with cortisone there was a marked improvement, which was thought to be associated with the cortisone. The cause of the patient's pyrexia is uncertain. There were no definite physical signs, apart from a few adventitious sounds in the lungs, and it seems unlikely that the toxaemia was due to infection and that the penicillin had anything to do with the dramatic recovery. It cannot, of course, be said with certainty that cortisone was responsible for the improvement. The other hormones had been given for some 48 hours previously, and it is possible that improvement was due to a delayed effect of the previous therapy, though the prompt response to cortisone following the very little change which had taken place during the previous therapeutic regime raised the strong possibility that the recovery was due to cortisone.

It is realized that this case is very far from proof that cortisone is a drug of choice in the treatment of acute Simmonds's disease crisis, but these observations have been recorded so that a wider trial can be given in future cases.

## A CASE OF SIMMONDS'S DISEASE WITH MENTAL SYMPTOMS

BY

**J. TODD, M.B., B.S., D.P.M.**

*Senior Registrar, Park Prewett Hospital, Basingstoke*

The recent advances in endocrine therapeutics have revived interest in the disorder known as Simmonds's disease. In the past the missed diagnosis was often condoned, if not excused, by the fact that no effective treatment was available, but this no longer holds true. Furthermore, the diagnostic difficulties have been considerably lessened by the brilliant studies of Sheehan, whose portrayal of the typical case is unlikely to be surpassed. The earlier textbook descriptions were misleading in that undue stress was laid on such inconstant signs as progeria, cachexia, and hypotension, whereas insufficient notice was taken of the accompanying mental disturbance. Sheehan and Summers (1949), in a full review of the disease, write: "In the later stages a number of patients present mental symptoms and are removed to asylums, where attention is focused more on the psychological than the physical aspects of the condition."

The case described below is of especial interest in that it was the mental, not the physical, symptoms which brought the patient into hospital.

### Case Report

A married woman aged 54 was admitted to hospital on February 3, 1950. She complained of depression, general weakness, and cramping pains in the calves. She was married in 1925 at the age of 29, and had had two uncomplicated pregnancies, in 1926 and 1929. In 1933 the birth of a stillborn child was followed by a severe haemorrhage, for which she was given an infusion of saline but no blood transfusion. Permanent amenorrhoea followed the post-partum haemorrhage. Coitus ceased as a result of both a loss in sexual appetite and a progressive shrinking of the vagina. Her axillary and pubic hair gradually disappeared, her head hair became dry and coarse, while her eyebrows grew steadily thinner. Her skin became dry and scaly. An insidious decline in her general health took place *pari passu* with the changes already described.

Since 1940 she had been subject to attacks of fainting and vague abdominal pain. From 1945 onwards her family noticed signs of increasing mental torpor and physical deterioration. She became slow in her speech and in the performance of simple routine tasks. She developed an inability to tolerate the vicissitudes of the climate, being prostrated by very hot or cold weather. Her cheeks, which were florid prior to the haemorrhage, assumed a remarkable pallor. Despite her failing health, she remained fairly cheerful until a few months before admission, when she suddenly became anxious and depressed. No marked loss of weight had taken place.

FIG. 1.—Photograph taken on March 22 (before treatment), showing scanty eyebrows and complete absence of pubic and axillary hair. Erythema ab igne is well shown on legs.

On admission she was noted to be in a fair state of nourishment. A striking degree of facial pallor gave rise to the suspicion that she had a severe degree of anaemia. Her eyebrows were scanty and the axillary and pubic hair absent (Fig. 1). Her skin was dry and wrinkled and showed a fine scaliness. Her fingernails were thin, dry, and brittle; they were not spoon-shaped. No abnormality was noted in the chest, abdomen, or central nervous system. The blood pressure was 140/80. The vagina admitted only the index finger. Her weight was 6 st. 4 lb. 10 oz. (40.2 kg.). Progeria was not in evidence. Pigmentation of the skin was absent, but erythema ab igne was conspicuous on the legs. The mental picture was one of slight retardation with depression and anxiety.

#### Investigations

On February 4 a blood count gave: red cells, 4,010,000 per c.mm.; haemoglobin, 85%; colour index, 1; white cells, 5,250 per c.mm. (polymorphs 28%, lymphocytes 67%, monocytes 3%, eosinophils 1%, basophils 1%). The corrected B.S.R. was 12 (Wintrobe). The W.R. was negative. *X*-ray studies of the skull (including the sella turcica), heart, and lungs showed no abnormality.

The 24-hour urinary excretion of 17-ketosteroids was 2.3 mg. The fasting blood-sugar and sugar-tolerance curve gave a fasting value of 100 mg. per 100 ml.; half an hour after 50 g. of glucose it was 100 mg; one hour later, 90 mg.; one and a half hours later, 80 mg.; two hours later, 80 mg.; two and a half hours later, 80 mg.

On March 27 the following results were obtained by a biochemical study of the blood: blood urea, 20 mg./100 ml.; blood cholesterol, 234 mg./100 ml. Serum sodium, 285 mg./100 ml.; serum potassium, 17.7 mg./100 ml.; serum

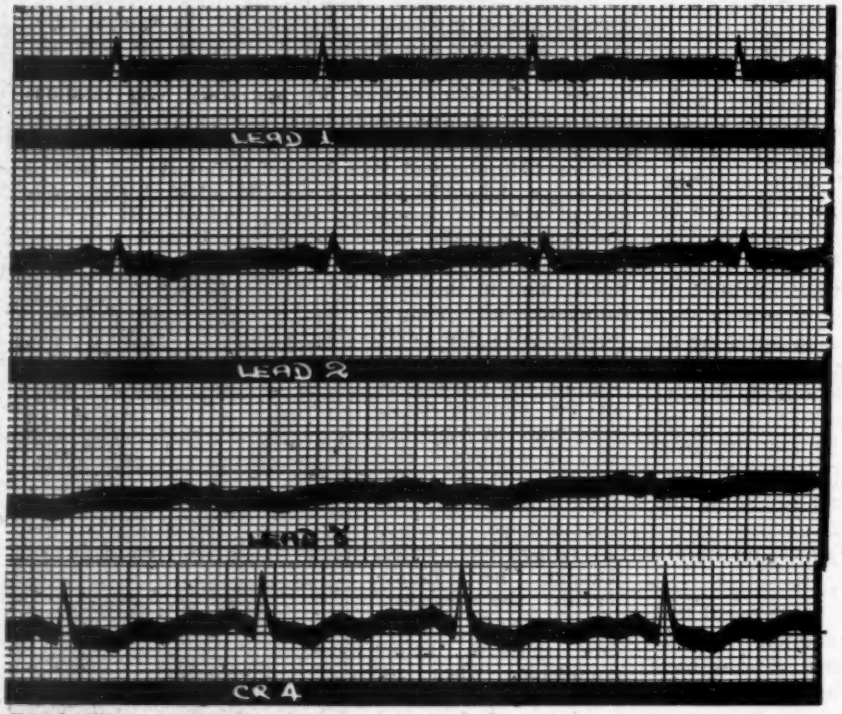


FIG. 2.—Electrocardiogram taken on March 27 (before treatment), showing low-voltage deflections and inverted T waves.

chlorides, 545 mg. (NaCl)/100 ml. An electrocardiogram taken on the same day showed a very low voltage with inverted T waves (Fig. 2).

Kepler's test (Robinson *et al.*, 1941) was performed on April 14 with the following results: "Whole night" urine, 14 oz. (400 ml.); "largest morning specimen," 3 oz.; blood urea, 30 mg./100 ml.; serum chloride (NaCl) 486 mg./100 ml.; urine urea, 1.3%; urine chloride (NaCl), 169 mg./100 ml. Factor "A"= 26.7. Kepler's test (I) was therefore positive; Kepler's test (II) was a doubtful positive.

The average pulse rate over a four-day period was 60 a minute. Free hydrochloric acid was present in the gastric juice. Psychometric testing (Wechsler–Bellvue) showed an intellectual deterioration of 11% after due allowance had been made for normal deterioration with age.

An attempt to estimate the B.M.R. failed owing to the inability of the patient to co-operate with the technicians. The insulin-sensitivity test of Fraser and Smith (1941) was not performed, as it was feared that a refractory hypoglycaemia might occur.

Little change was observed in the patient's physical condition during the three-months interval between her admission and the beginning of treatment on May 8. The mental picture remained that of an agitated melancholia with ideas of unworthiness.

### Treatment and Progress

Hormone treatment was started on May 8, her weight then being 6 st. 3 lb. 4 oz. (39.6 kg.). Sublingual tablets of methyl testosterone, 25 mg. daily, and thyroid, *B.P.*, ¼ gr. (16 mg.). daily, formed the initial basis of the treatment.

By September 8 she was taking each day oral methyl testosterone, 35 mg., thyroid 1¼ gr. (81 mg.), and D.C.A. linguets, 1 mg. A blood analysis and an electrocardiogram taken at this time showed that a great improvement had occurred. The blood analysis gave: blood cholesterol, 133 mg./100 ml.; serum sodium, 336 mg./100 ml.; serum potassium, 18 mg./100 ml.; serum chlorides (NaCl), 600 mg./100 ml. The electrocardiogram showed a satisfactory voltage with upright T waves (Fig. 3).

When discharged she was taking sublingual methyl testosterone 30 mg. (20 mg. mornings, 10 mg. afternoons), and thyroid 1 gr. (65 mg.). The D.C.A. linguets had been discontinued, as she had had an implant of 200 mg. on October 3.

Her response to treatment was immediate and dramatic. By the end of the first week she looked more animated and seemed much quicker in her reactions. On May 31 her husband wrote an enthusiastic letter describing the improvement in her mental state and spoke of "her new-found capacity for laughter."

When she left hospital on October 8 all signs of mental disorder had gone. The Wechsler–Bellvue psychometric tests had been repeated and had failed to detect intellectual deterioration above that normal for her age. The hair of her head had acquired the normal greasiness and lustre. The skin was now moist and no longer scaly. The nails had become normal. The hair in the axillae was still absent, but a remarkable regrowth of the pubic hair had taken place (Fig. 4). Her weight was now 6 st. 12 lb. 12 oz. (43.9 kg.), representing a gain of 9 lb. 8 oz. (4.3 kg.). She had experienced a marked increase in strength since starting treatment.

FIG. 3.—Electrocardiogram taken on September 8 (after treatment), showing satisfactory voltage deflections with upright T waves.

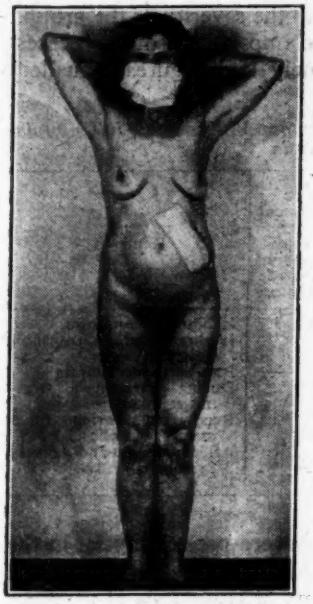

FIG. 4.—Photograph taken on October 6 (after treatment), showing a remarkable regrowth of pubic hair. The dressing on the abdomen covers the D.C.A. implant.

A point worthy of note was the superiority of sublingual to swallowed testosterone; the patient was emphatic in her assurance that 25 mg. of sublingual testosterone was superior to a swallowed dose of 35 mg.

### Discussion

In this case the history and clinical appearances were quite typical of Simmonds's disease arising from a subtotal pituitary necrosis produced by a post-partum haemorrhage. It would appear that the pituitary gland is peculiarly sensitive to the effects of haemorrhage at the moment of parturition; at other times it tends to escape destruction. Hobson and Fraser (1949) have, however, reported a case of Simmonds's disease following haematemeses due to a gastric ulcer.

A feature worthy of comment was the presence of well-marked erythema ab igne, which according to Sheehan and Summers (1949) " is almost always present on the legs of the female patients," the excessive sensitivity to cold causing these patients to sit huddled over a fire. The figures obtained for the blood-sugar and sugar-tolerance curve are similar to a set quoted by Farquharson (1950).

A noteworthy factor in the present case was the striking improvement in the wave pattern of the electrocardiogram after endocrine treatment, which did not include the use of extra salt. The abnormal cardiogram is not necessarily produced by the hypothyroid element in the disorder, but may arise from the secondary adrenal insufficiency. It is reported that cortisone has beneficial effects on the cardiogram in this type of case (Somerville, 1950).

Finally, it is interesting to speculate on the incidence of Simmonds's disease in the light of modern knowledge. In the past, spontaneous cures must have occurred as a result of the beneficial effects of subsequent pregnancies (Sheehan and Murdoch, 1938). In the future, Simmonds's disease due to post-partum haemorrhage may disappear following improvement in the blood transfusion and obstetric services.

### Summary

A case of Simmonds's disease due to post-partum haemorrhage is described. The fact that the dominating symptoms were mental is stressed. An account, supported by biochemical data, is given of the beneficial effects of treatment with methyl testosterone, thyroid, and deoxycortone acetate.

My thanks are due to Dr. I. Atkin, physician-superintendent, for his encouragement and permission to record the case; and to Dr. J. Harkness for the steroid estimations. I am indebted to Dr. H. S. le Marquand for his practical assistance and advice. I am also grateful to those nurses and technicians of Rooksdown House and Park Prewett Hospital who helped with the work involved.

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# PLASMA PENTOSE LEVELS IN PRE-ECLAMPSIA AND THEIR AETIOLOGICAL SIGNIFICANCE

BY

**H. N. GREEN, M.A., M.D., M.Sc.**

**J. D. HOPEWELL, M.B., Ch.B., B.Sc.**

AND

**C. J. THRELFALL, B.Sc.**

*(From the Department of Pathology, University of Sheffield)*

One fact on which all agree is that overstretching of the wall of the pregnant uterus, from whatever cause, plays a decisive initiating part in the pre-eclamptic state. Since we (Green, 1943; Green and Stoner, 1950a, 1950b) have studied extensively the local and general effects of muscle ischaemia it was natural to wonder whether this overstretching resulted in a functional ischaemia of the pregnant uterus. If this were so it would then seem highly likely that a metabolite(s) from ischaemic muscle or placenta was the exciting cause of the pre-eclamptic and eclamptic state. As we shall see, this proved to be no new hypothesis, but all the evidence in its favour was circumstantial.

We were able to tackle the problem somewhat more directly when we had shown that after large-scale ischaemia of voluntary muscle adenine nucleotides and their breakdown products were increased in the blood (see Green and Stoner, 1950a). As these are pentose compounds, the most useful method of estimation when haemolysis can be avoided is the chemical determination of the total pentose and phosphorylated pentose contents of the plasma. The figures thus obtained give no precise information about the nature of these pentose compounds, but when significantly increased they appear to indicate that a mass of tissue with an inadequate blood supply exists, or recently existed, in the body (see Green *et al.*, 1949a). For these reasons the methods were applied to the study of pre-eclamptic patients solely for the purpose of providing practical evidence for or against the hypothesis that utero-placental ischaemia is the basic pathological state underlying all the features of the syndrome. Seven years ago, with Dr. M. Bielschowsky's help, a few observations were made and the results were such that further work seemed desirable. We are now able to report on more recent findings in a series of normal and pre-eclamptic pregnant women, together with a few cases of frank eclampsia.

### Chemical Methods

The blood, after collection in waxed 15-ml. centrifuge tubes containing 1 mg. of heparin, is centrifuged. The plasma, after precipitation with an equal volume of 10% trichloracetic acid, is shaken, stood for one hour, and then centrifuged. The supernatant fluid is removed.

*Total Pentose.*—This is a modification of the method of Mejbaum (1939): 0.5 ml. of the supernatant fluid is diluted with water to 2 ml., and 2 ml. of orcinol reagent (1% recrystallized orcinol in concentrated HCl containing 2 vols. 10% $FeCl_3.6H_2O$ in 100 ml. of acid) is added. The mixture is shaken and then heated for 20 minutes in a boiling water-bath. It is then cooled, filtered (Whatman 42) if turbid, and compared with standard ribose solutions on the Hilger absorptiometer.

*Phosphorylated Pentose.*—Supernatant fluid, 0.5 ml., is added to 10 ml. of water in a 15-ml. centrifuge tube followed by the addition of 1 ml. of 1.5% pure cadmium chloride solution and 2 ml. of 5% NaOH solution. The mixture is well shaken, allowed to stand for two hours, and then centrifuged. The supernatant fluid is poured off and the inverted tube allowed to drain for five minutes. Orcinol reagent, 2 ml., is added to the cadmium precipitate, and the volume is made up to 4 ml. with water. The pentose estimations are then made as described for total pentose (Bielschowsky, 1947).

## Clinical Assessment

The precise degree of severity of the pre-eclamptic state is difficult to assess. It is a labile condition, varying almost from hour to hour. A woman admitted as a severe case may, when the blood sample is taken a few hours later, be actually recovering rapidly. The three gradings we have attempted—of severe (+++), moderate (++), and mild (+)—are based on the clinical findings at the time of admission to hospital. In the severe grade were included cases of frank eclampsia and those with pronounced hypertension (systolic B.P. 180+), and both severe oedema and albuminuria. The other cases were graded relatively to these. The borderline cases, particularly evident between moderate and mild, were included in one of the two grades alternately. Attempts at a more precise grading on a blood-pressure basis were made and abandoned. When available, normal pregnant women were bled in the week of pregnancy corresponding to that of a recent pre-eclamptic case.

## Results

Whilst it was soon obvious that the plasma pentose content often rose steeply in severe pre-eclampsia it was just as obvious that some cases in which the diagnosis was not in doubt were providing figures within the normal range. Interest therefore centred on the statistical analysis of the group figures. Such an analysis (Table I) leaves little doubt that in this series of 59 toxaemic and 37 normal pregnancies there is a significant rise in both the total and the phosphorylated pentose in the toxaemic group as a whole. Moreover, the extent of the rise increases with the severity of the group. It reaches its peak in frank eclampsia, two of such cases (see Table II) giving extremely high figures, equalled only by one other, a case of severe pre-eclampsia, in the whole series. A detailed analysis of the individual figures is unnecessary here, for it is obvious at a glance that a biochemical diagnosis could not be made with any certainty in the one instance, the borderline case, where it might have practical value.

TABLE I.—*Comparison between Mean Plasma Pentose Values (mg./100 ml.) in Normal Pregnancies and in Toxaemic Pregnancies of Differing Grades of Severity*

| | No. in Group | Mean Total Pentose | Mean Phosphorylated Pentose |
|---|---|---|---|
| Controls .. .. | 37 | 3·71 (3·46, 3·97) | 1·91 (1·73, 2·09) |
| + .. .. .. | 24 | 4·23 (3·74, 4·72) | 2·19 (2.02, 2·36) |
| ++ .. .. .. | 23 | 4·55 (4·09, 5·02) | 2·45 (2·07, 2·84) |
| +++ .. .. .. | 12 | 7·02 (5·24, 8·81) | 3·87 (2·57, 5·17) |

An overall F. test on the differences between the groups shows that in both the case of total pentose and that of phosphorylated pentose the differences can be regarded as significant, with $P<0.01$. The variances of the groups cannot be regarded as equal, and accordingly the 95% fiducial limits (as given in parentheses) for the various means have been calculated from the t-distribution as represented by the observations within the particular grou .

TABLE II.—*Individual Plasma Pentose Values (mg./100 ml.) in Eclampsia*

| Case | Before Treatment | | During or After Treatment | | Remarks |
|---|---|---|---|---|---|
| | Total Pentose | Phosphorylated Pentose | Total Pentose | Phosphorylated Pentose | |
| 1 | 12·0 | 6·9 | 5·8 | 3·3 | 10 hours post partum |
| 2 | 10·6 | 6·8 | 7·0 | 6·5 | 19 hours after Stroganoff treatment |
| 3 | 5·3 | 2·0 | — | — | Post-partum eclampsia |
| 4 | — | — | 4·7 | 2·2 | During Stroganoff treatment. Died |
| 5 | — | — | 4·7 | 3·4 | Recovering during treatment. Systolic B.P. 145 |
| 6 | — | — | 3·2 | 2·1 | After treatment and delivery Systolic B.P. 100 |

It will be obvious that most of the cases showing very high values for both total and phosphorylated pentose belong to the severe group. In fact, only one of the twelve cases gave figures within the normal range, and in this instance the blood sample was a post-partum specimen. Two cases of accidental haemorrhage complicating severe pre-eclampsia gave the high figures of 6.4 and 2.5 and 7.6 and 2.9 for total and phosphorylated pentose. In the latter case (not included in the present series) death occurred after bilateral cortical necrosis.

The six cases of frank eclampsia (Table II) provided data which at first sight look rather anomalous, for in two cases the values are tremendously high and in the rest are much lower or normal. In only three (Cases 1 to 3) were blood samples obtained before active treatment was started, and in the one (Case 3) giving a comparatively low value the diagnosis was somewhat doubtful. The lower values were otherwise all in cases which were under treatment or, as in Case 6, had recovered after treatment. We have not yet enough follow-up figures in toxaemic cases, but so far as they go they suggest that high pentose values rapidly fall with clinical improvement, and Cases 1 and 2 illustrate this tendency. In eclampsia $MgSO_4$ treatment may, possibly by dilating the uterine vessels and/or relaxing the uterine muscles, relieve the uterine ischaemia and thus cause a rapid fall in the plasma pentose. Evacuation of the uterus would of course have the same effect. Incidentally, the fact that death occurred in Case 4 suggests that the pentose values have no prognostic significance.

## Discussion

We have seen that there is a statistically significant increase in the content of total and phosphorylated pentose in the blood plasma of pre-eclamptic and eclamptic patients. In individual cases the figures may reach the relatively enormous values of three or more times the normal. The main importance of these findings is in their possible bearing on the aetiology of the pre-eclamptic state. There is good evidence for the assumption that this rise in the plasma pentose is the direct

consequence of a state of large-scale tissue ischaemia in or recently in existence. The findings of Stoner and Green (1944, 1945), that in experimental limb ischaemia, both in animals and in man, there is a raised adenosine equivalent in the whole blood, fall into line with the plasma pentose observations previously mentioned. There are also the large-scale observations on battle casualties (Green *et al.*, 1949b) which revealed a significant rise in the plasma pentose fractions, believed to be the result of ischaemia in the injured tissues. Incidentally, it is noteworthy that the average control value (3.7 mg. per 100 ml.) for total pentose in this series of pregnant women is exactly that of 164 healthy young soldiers.

The precise degree of ischaemia necessary to produce a rise is not known, but it seems likely that a degree which diminishes the oxidative breakdown of carbohydrate even slightly is associated with this release of pentose compounds from the tissue.

Here the most important question is what tissues are involved. There is no evidence of any reduction, but rather of an increase, in blood flow to those tissues (for example, brain, kidney, liver, limbs, skin) which have been studied in pre-eclampsia (see Kellar, 1950), but nothing definite is known about uterine blood flow even in normal pregnancy. In view of the overwhelming importance of uterine overstretching in causation, it would seem that these plasma pentose values are prima facie evidence for the existence of a reduced blood flow, relative to requirements, in the uterus and placental site of the pre-eclamptic patient. Even if peripheral vasoconstriction exists, for which there is no evidence, it is not a likely cause of the raised pentose values, for they show no precise correlation with the degree of hypertension. Moreover, none of five hypertensive women in the control group showed pentose values outside the normal limits.

Of course, if the very high values had been confined to cases of eclampsia alone it might have been argued that the convulsive spasms could temporarily produce relatively ischaemic muscle masses and thus cause the rise in plasma pentose. Though such an effect would probably be of short duration it might have contributed to the great rise observed in the untreated cases of eclampsia. It could not be responsible for the whole, for apart from the fact that big rises were observed in pre-eclampsia, relatively high values were found in eclampsia many hours after the last convulsion.

There is no need here to review again the whole vexed question of the aetiology of this syndrome. Browne (1944) has provided a fairly recent critical review and there is still more recently the Ciba Foundation Symposium (1950). We came to the view that utero-placental ischaemia was a likely cause of the disease because of (1) its relation to overstretching of the uterus; (2) its association with the erect posture; and (3) the profound antidiuretic effect of tissue ischaemia. According to Eastman (1950) the hypothesis was first advanced in clean-cut fashion by J. Young in 1914, but Page (1939, 1948) has been foremost in reasoned advocacy for the hypothesis. He suggests that there exists a relative maternal ischaemia of the placenta. This leads to premature degeneration of the trophoblast with the liberation of toxic proteins. He lists possible causes of relative ischaemia as follows: increased hydrostatic pressure within the uterus—hydramnios, twins, triplets, increased intra-abdominal pressure; lack of stretching—primiparity (particularly early and late), obesity, short stature; diffuse mechanical compression — labour; vasoconstriction of spiral arterioles—emotional strain, shock; systemic arterial disease—pre-existing hypertension, nephritis, diabetes; and severe maternal anaemia—hookworm, sickle-cell. The evidence for the hypothesis is mainly circumstantial—for example, the foetus often dies and its rate of growth is reduced.

Attempts have been made to find experimental support for the idea, and Page, with others (Ogden *et al.*, 1940) described a delayed rise in blood pressure after acute uterine ischaemia in pregnant dogs, and Bastiaanse and Mastboom (1950) have provided similar though not very convincing evidence. Page holds that toxic proteins from an ischaemic placenta could account for postpartum eclampsia, and in general puts forward a convincing argument for the hypothesis. He agrees that proof is lacking, for efforts to produce chronic ischaemia in the uterus of rabbits without death of the foetus were unsuccessful. Eastman (1950) also marshals well the arguments in favour of utero-placental ischaemia. He mentions the factor of erect posture, which has always seemed to one of us (H. N. G.) of paramount importance, for pre-eclampsia is a peculiarly human disease, and its importance is probably indicated by the simple fact that the most successful therapy in early cases is rest in bed.

Beker (1948) has pointed out that the main branches of the uterine artery come off at a hairpin bend after it enters the cervix and, moreover, in the upright posture are working against gravity. All this is most suggestive, but, as Eastman writes, "although the theory of uterine ischaemia has much in its favour . . . it has not yet been proved. No placental pressor substance has yet been demonstrated." Since then Thompson and Tickner (1949) have demonstrated *in vitro* the presence of a highly active mono-amino-oxidase in placental tissue capable of inactivating vasoconstrictor amines. The activity of this oxidase falls very strikingly with falling oxygen tension. Although no claim is made, this finding might account for the hypertension following placental ischaemia.

Here direct rather than circumstantial evidence in favour of the hypothesis is presented. The weak point is that complete individual correlation in our findings is lacking. This discrepancy, also noted in many other types of blood and urine assays, is, in our opinion, probably due to the great lability of the condition. Once the patient is recumbent the presumed utero-placental ischaemia could diminish or disappear rapidly, and so could the presumed biochemical indicator of its presence, for pentose compounds when injected disappear very rapidly from the circulation (see Green and Stoner, 1950a).

The chemical nature of the pentose compounds released from ischaemic muscle has been discussed before (Green and Stoner, 1950a, 1950b, 1951). Whether they play any part in the clinical picture of pre-eclampsia is at present pure guesswork. They could hypothetically be concerned in pre-eclamptic oedema, as the adenine nucleotides have a strong antidiuretic action (Green and Stoner, 1950a). It should be mentioned also that the adenine nucleotides, particularly A.T.P., strongly stimulate contractions in the pregnant uterus (Whiteley and Green, 1951). As excessive discharge of placental thromboplastin has been claimed to be an important factor in the pathogenesis of eclampsia (Schneider, 1950), it may be of some relevance that the thromboplastic activity of muscle rises steeply during and

following ischaemia (Stoner and Green, 1947, 1948, 1951), and that the toxic effects of these pentose compounds are strongly potentiated by thromboplastin (Green and Stoner, 1947). We have, however, no direct evidence at all that pentose compounds, thromboplastin, or both are concerned in the mechanism.

Indeed, the pentose compounds are likely to be vasodepressor and most certainly do not provide the hypertensive agent, the nature of which remains the crux of the problem. The formation of this agent is probably an adaptive mechanism to preserve an adequate blood supply to the placental site. By exclusion the placenta seems to be its most likely source of origin, for ischaemic muscle does not release pressor substances, and the common occurrence of pre-eclampsia when a hydatidiform mole is present excludes the foetus as a source.

Finally, we present some new arguments for the ischaemic theory, arising directly from findings of the Sheffield Traumatic Shock Team. Muscle ischaemia may lead to a profound general interference with carbohydrate utilization. Any superadded disturbance in carbohydrate metabolism strongly increases the harmful effects of the post-ischaemic state. In regions where pellagra and beriberi are endemic the incidence of pre-eclampsia rises steeply, and diabetics are known to be more prone. All these diseases are manifestations of faulty carbohydrate utilization. In striking contrast general undernutrition, as distinct from specific vitamin deficiencies, reduces susceptibility, possibly by diminishing the growth rate of the foetus.

Of the many environmental factors affecting the bodily response to tissue ischaemia, the air temperature is perhaps the most important. A fall of a degree or two may convert a mild into a severe, even fatal, reaction. Though not proved, there is a strong impression that pre-eclampsia occurs most commonly when there is a sudden change to cooler weather.

The direct evidence presented here, supported by such a weight of indirect evidence, strongly favours the ischaemic utero-placental hypothesis. With H. J. Whiteley, experimental work directly testing the hypothesis is in progress, and when this is reported fresh data and points merely mentioned here will be elaborated.

**Summary**

There was a statistically significant rise in the average pentose and phosphorylated pentose content of the blood plasma in a group of women with pre-eclampsia.

The degree of the rise showed a correlation with the severity of the clinical condition, reaching a peak in frank eclampsia. It had no individual but only a group significance.

It is shown that this rise is probably due to relative utero-placental ischaemia in the pregnant uterus. The hypothesis that this is the proximate cause of pre-eclampsia is now supported by direct evidence. Other facts, some new, are presented which give strong indirect support to this hypothesis.

The nature of the substances which might be released from an ischaemic placenta and/or uterus is briefly considered. The important hypertensive agent, probably derived from ischaemic placenta, has still to be identified.

The Medical Research Council was responsible for the expenses of this investigation. We are indebted to Mr. R. F. Wrighton, of the Department of Social Medicine, Sheffield, for his valuable statistical help, to Dr. H. B. Stoner for his willing collaboration in closely related investigations, and to the late Professor Chisholm and the staff of the Jessop Hospital for Women for their co-operation.

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# HYPOGLYCAEMIA IN TREATMENT OF RHEUMATOID ARTHRITIS

BY

**G. D. KERSLEY, M.D., F.R.C.P.**

**L. MANDEL, M.B., M.R.C.P.**

**M. R. JEFFREY, M.B., M.R.C.P.**

**E. BENE, M.D.**

AND

**K. B. TAYLOR, B.M., M.R.C.P.**

*(From the South-west and Oxford Regional Rheumatism Research Unit, Royal National Hospital for Rheumatic Diseases, Bath)*

Insulin has been used in three ways in an attempt to improve rheumatoid arthritis: in small dosage to improve metabolism and increase appetite (Copeman, 1931); in conjunction with cortisone in order to attempt to spare protein and to make carbohydrate available at the cell face (Henderson *et al.*, 1951); and to stimulate the pituitary-adrenal complex (Kersley *et al.*, 1950) by means of hypoglycaemia.

In October, 1950, we published a report on the treatment of a pilot series of 40 cases of rheumatoid arthritis with hypoglycaemia. Since this communication 32 further cases have received similar treatment, making a total of 72. All these cases have been followed up for at least two months, and some in which improvement has continued or been maintained, have been followed up for 12 months. Some of the patients who improved at the end of treatment and then relapsed were given a second course of hypoglycaemia. Some of the patients who did not respond

to insulin were given a short course of A.C.T.H. and cortisone, and the clinical response to these hormones was compared with that of another group who improved and later relapsed after hypoglycaemic treatment. A few patients who improved with hypoglycaemia were given minimal doses of these hormones immediately after treatment, in an endeavour to maintain improvement, and were compared with a similar group who received the same dosage of hormones only. As all patients who received treatment were also given a basic regime of rest and physiotherapy in hospital, a series of controls who received this basic regime alone were similarly assessed for comparable periods.

The technique of treatment and the method of clinical assessment were similar to those previously reported. A good hypoglycaemic reaction was indicated clinically by flushing, sweating, weakness, and drowsiness, and the dose required to produce this varied widely, from 16 to 120 units. Some patients were treated for six weeks in order to determine if a change in tolerance to insulin developed, but when once stabilized it was found that little change in dosage for any individual patient was necessary.

Pathological investigations (in addition to routine E.S.R. and Hb) in some cases included estimations of eosinophil counts, potassium and sulphydryl levels in the serum, 17-ketosteroids and cortin-like bodies in the urine, and the excretion of potassium and phosphate in the urine.

## Results

The results are summarized in Table I. Of the 72 cases treated, 82% had improved after treatment, 44% markedly so, but two months later these figures had deteriorated to 58% and 30% respectively, owing to relapses. Seven of the first 40 cases were greatly improved and appeared to be in complete clinical remission six months after completing treatment. These figures may be compared with a control series of 22 subjects who received physical treatment only in hospital. In this control series, 78% were improved on discharge from hospital, but only 14% markedly so. Two months later the figures were 74% and 32% respectively. In the series treated with hypoglycaemia, those with a history of the disease being present for one year or less reacted slightly better than those of longer duration.

From examination of the Table it may be seen that the increase in weight of the cases whilst under treatment was considerable. 96% of cases gained more than 3 lb. (1.4 kg.) and 6% more than 15 lb. (6.8 kg.). Two months later 79% were more than 3 lb. (1.4 kg.) heavier than before treatment. There was, however, no correlation between improvement and previous loss of weight as has been suggested by the somewhat astonishing gain in weight during treatment in nearly all cases.

There was a tendency to decrease in the sedimentation rate. Immediately after treatment 53% showed a decrease of more than 10 mm. (Westergren) and 27% showed a rise of more than 10 mm. Two months later those with a corresponding fall in E.S.R. were reduced to 43% and those with a corresponding rise increased to 37%.

There did not appear to be any beneficial effect on the haemoglobin levels. Only 20% of cases showed a rise of more than 1 g. per 100 ml., whereas in 43% the haemoglobin fell by more than 1 g. per 100 ml. Two months later the corresponding figures were 35% and 42%.

TABLE I.—*Effect of Three Weeks' Course of Hypoglycaemia on Rheumatoid Arthritis*

*Clinical Condition*

| | No. of Cases | Complete Remission | Much Improved | Improved | Unchanged | Deteriorated |
|---|---|---|---|---|---|---|
| At end of treatment .. | 72 | 7 (11%) | 32 (44%) | 27 (38%) | 11 (15%) | 2 (3%) |
| Two months later .. .. | 64 | | 12 (19%) | 18 (28%) | 17 (26·5%) | 10 (15·5%) |

*Effect on Weight*

| | No. of Cases | Loss | No Change | + 3–9 lb. (1·4–4·1 kg.) | + 9–15 lb. (4·1–6·8 kg.) | + 15 lb. (6·8 kg.) |
|---|---|---|---|---|---|---|
| At end of treatment .. | 69 | 1 (1·4%) | 2 (2·8%) | 38 (55%) | 24 (35%) | 4 (5·8%) |
| Two months later .. .. | 60 | 4 (6%) | 9 (15%) | 27 (46%) | 16 (27%) | 4 (6%) |

*Effect on Sedimentation Rate*

| | No. of Cases | Decrease | | | No Change | Increase | | |
|---|---|---|---|---|---|---|---|---|
| | | 40 | 20–40 | 10–20 | | 10–20 | 20–40 | 40 |
| At end of treatment .. | 67 | 4 (6%) | 15 (22·5%) | 17 (25%) | 13 (19·5%) | 10 (15%) | 5 (7·5%) | 3 (4·5%) |
| Two months later .. .. | 62 | 4 (6·5%) | 9 (14·5%) | 14 (22·5%) | 12 (19·5%) | 8 (13%) | 10 (16%) | 5 (8%) |

*Effect on Haemoglobin*

| | No. of Cases | Increase | | | No Change | Decrease | | |
|---|---|---|---|---|---|---|---|---|
| | | 4 g. | 2–4 g. | 1–2 g. | | 1–2 g. | 2–4 g. | 4 g. |
| At end of treatment .. | 67 | 2 (3%) | 4 (6%) | 7 (10·5%) | 25 (37·5%) | 16 (23·5%) | 9 (13·5%) | 4 (6%) |
| Two months later .. .. | 62 | 1 (1·5%) | 11 (18%) | 10 (16%) | 14 (22·5%) | 12 (19·5%) | 13 (21%) | 1 (1·5%) |

*Controls: Clinical Conditions*

| | No. of Cases | Complete Remission | Much Improved | Improved | Unchanged | Deteriorated |
|---|---|---|---|---|---|---|
| At end of treatment .. | 22 | 1 (5·3%) | 3 (13·5%) | 14 (64%) | 4 (18%) | 1 (4·5%) |
| Two months later .. .. | 19 | | 5 (26·3%) | 8 (42·1%) | 4 (21%) | 1 (5·3%) |

A second course of hypoglycaemia was given to 12 patients who had improved after a first course but had later relapsed after periods varying from 4 days to 13 weeks. Details are given in Table II. The striking

TABLE II.—*Comparison of Results of First and Second Courses of Hypoglycaemia*

| Case No. | Duration of 1st Course | Clinical Change After 1st Course | Time Interval of Relapse | State of Relapse | Time Interval Between 1st and 2nd Courses | Duration of 2nd Course | Clinical Change After 2nd Course |
|---|---|---|---|---|---|---|---|
| 2 | 13 days | ++ | 5 weeks | − | 13 weeks | 5 days | + |
| 3 | 13 ,, | ++ | 4 ,, | 0 | 13 ,, | 5 ,, | 0 |
| 21 | 20 ,, | + | 8 ,, | − | 15 ,, | 14 ,, | 0 |
| 23 | 20 ,, | ++ | 13 ,, | + | 18 ,, | 15 ,, | ++ |
| 26 | 18 ,, | ++ | 3 ,, | − | 8 ,, | 20 ,, | + |
| 33 | 19 ,, | ++ | 10 days | 0 | 8 ,, | 15 ,, | + |
| 38 | 20 ,, | ++ | 7 ,, | 0 | 9 ,, | 10 ,, | 0 |
| 40 | 15 ,, | ++ | 14 ,, | 0 | 8 ,, | 15 ,, | 0 |
| 51 | 20 ,, | ++ | 4 ,, | 0 | 15 ,, | 30 ,, | ++ |
| 65 | 15 ,, | + | No relapse | | 6 ,, | 30 ,, | 0 |
| 69 | 15 ,, | + | 3 weeks | 0 | 7 ,, | 20 ,, | 0 |
| 5 | 19 ,, | + | 10 ,, | − | 8 months | 15 ,, | ++ |

feature is that only six patients improved at all, and of these only three improved as much as or more than with the first course.

During treatment with hypoglycaemia 35 out of 36 cases showed a decrease in the level of circulating eosinophils four and a half hours after maximal hypoglycaemia, as previously reported by us, but there was no clear correlation between this eosinopenia and either the clinical results or the Thorn test with A.C.T.H.

Estimations of the 17-ketosteroid and cortin-like bodies in the urine were carried out on nine cases, but in only one was there an apparent increase in both these steroids, and in one the cortins only.

There appeared to be a significant increase in potassium excretion in the 24-hour specimens of urine in four out of six cases, the average figure being 2.7 g., whereas the average excretion in control periods was 1.57 g. There was also a decrease of more than 50% in the phosphate excretion during the period of hypoglycaemia (but not over a 24-hour period) in four out of the five cases in which this determination was carried out.

The serum potassium was lowered at the height of hypoglycaemia in 34 out of 36 cases, but became normal within four hours. The serum sulphydryl content did not appear to be affected.

### Insulin and A.C.T.H.

An attempt has been made to compare the clinical effects upon individual cases of treatment with hypoglycaemia and A.C.T.H. Three cases which had responded well to insulin and then relapsed, and three cases which had failed to respond to insulin, were each given similar short courses of A.C.T.H. (The usual experimental course consisted of 100 mg. in divided dosage for four days and was then modified as clinically indicated.) From the Chart it will be seen that the three cases (1, 2, and 3) which had responded to insulin reacted excellently to A.C.T.H. Those cases (4, 5, and 6) in which arthritis had not improved with insulin in hypoglycaemic dosage responded poorly or not at all to A.C.T.H. In one case (No. 5) which had deteriorated during insulin treatment there was no response when the dose of A.C.T.H. was raised to 400 mg. daily, but every case except one (Case 6) responded to cortisone. Four cases which had responded to hypoglycaemia were immediately given 20 mg. of A.C.T.H. daily and one improved still further and two retained their improvement. Four similar cases which had not received insulin had a similar course of A.C.T.H., two improving very slightly.

### Discussion

No definite conclusions can be drawn from our findings on the mode of action of hypoglycaemia in rheumatoid arthritis, but in this connexion the work of Vogt (1950) may be quoted. She found that only A.T.P. or a very high concentration of potassium was effective in stimulating the perfused adrenal cortex isolated from pituitary effect. Adrenaline, which is produced by hypoglycaemia, has been shown experimentally to stimulate A.C.T.H. production, but clinically the results have not been dramatic, though Bliss *et al.* (1951) showed interesting results in normal subjects. After denervation of the adrenals, Vogt has shown that hypoglycaemia will still cause increased production of A.C.T.H., possibly through a second mechanism of reduction of circulating corticoids.

In our cases the marked reduction of circulating eosinophils in nearly all cases suggests pituitary–adrenal stimulation; the changes in potassium levels and excretion are compatible with this hypothesis, and we feel that the steroid excretion results do not rule this out.

Comparison of the figures of very marked improvement directly after treatment (44%) and two months later (30%) with those in the control series (14% and 32%) is such as one might expect with the use of medium doses of A.C.T.H. Again, the fact that the degree of clinical response to insulin corresponded very closely to the response to A.C.T.H. suggests that hypoglycaemia may have a pituitary-stimulating effect.

From the practical point of view we feel that hypoglycaemic therapy, although more difficult to administer than A.C.T.H. treatment, has much the same advantages and disadvantages, except that it is doubtful whether the response obtained by larger doses of A.C.T.H. can be obtained. This "treatment" may therefore be regarded as having a limited practical value in tiding over a temporary relapse, particularly if this has been occasioned by some temporary or removable factor and in conjunction with other methods in getting some mild cases back to work. In such cases it may produce a complete remission, as occurred in seven out of our first 40 cases so treated.

It is obviously not applicable in the third practical role of A.C.T.H. in rheumatoid arthritis—that is, tiding over surgical and manipulative intervention.

### Summary

Of 72 cases treated by hypoglycaemia 82% were temporarily improved, 44% markedly so. The improved figure had dropped to 58% in two months, but seven had progressed to complete remission after six months.

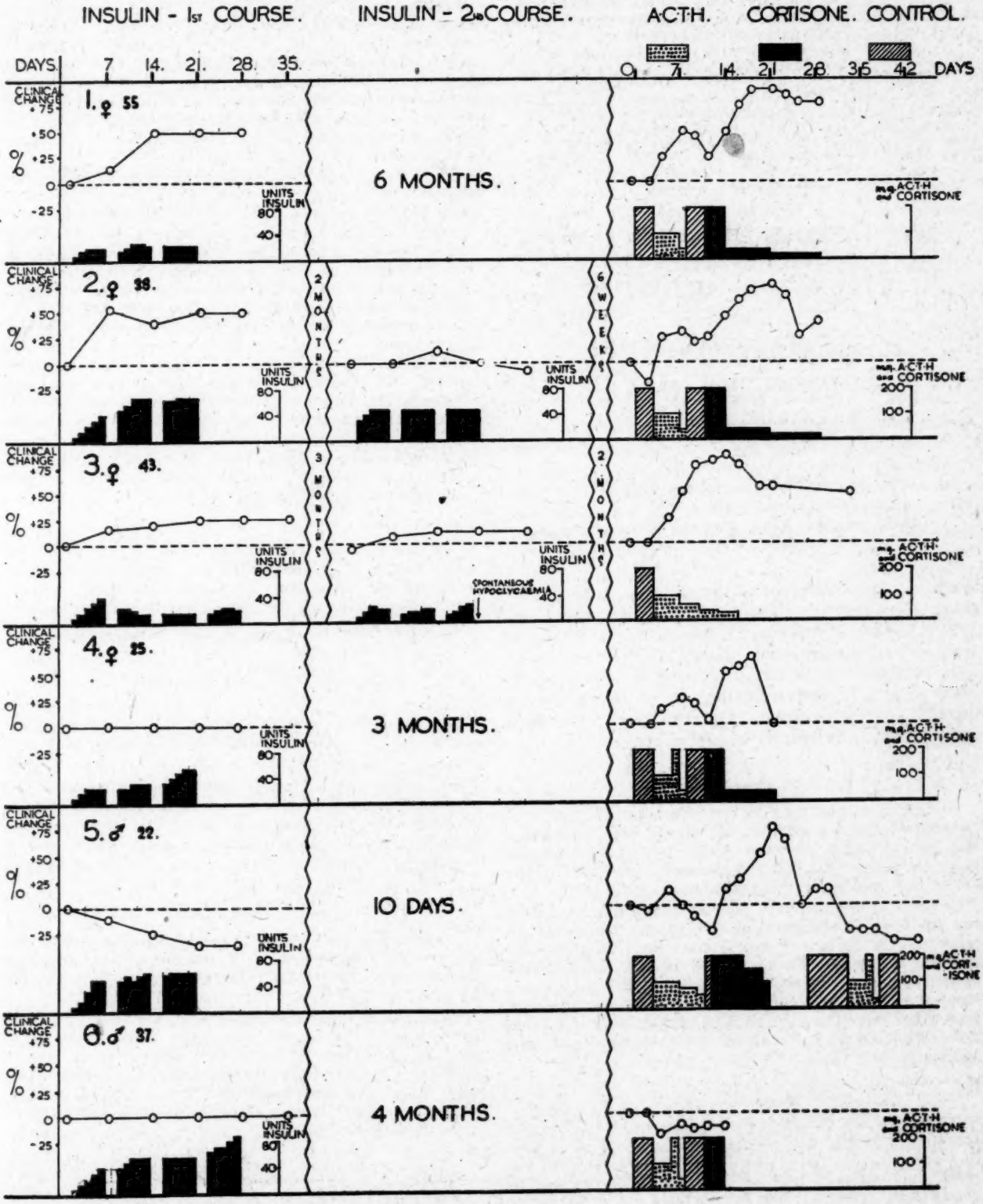
In a control series, without insulin therapy, 78% improved on a similar hospital regime but only 14% markedly.

A second course of treatment had less effect than the first.

Gain in weight was considerable and occurred in all but three cases; there was a tendency to improvement in the sedimentation rate but not in the haemoglobin level.

Reduction in circulating eosinophils occurred almost without exception. Observations on changes in potassium, phosphate, and steroid excretion were made.

# COMPARISON OF THE CLINICAL EFFECTS OF INSULIN WITH A·C·T·H AND CORTISONE



The clinical response to hypoglycaemia was compared with subsequent A.C.T.H. treatment and was found to correlate closely.

The possible mechanism and practical value of hypoglycaemic therapy in rheumatoid arthritis are discussed.

We would like to express our appreciation of the help given by the nursing and laboratory staff of the Royal National Hospital for Rheumatic Diseases, and of the grant made by the Empire Rheumatism Council towards laboratory expenses.

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# SPONTANEOUS HYPOGLYCAEMIA AFTER INSULIN THERAPY IN RHEUMATOID ARTHRITIS

BY

G. D. KERSLEY, M.D., F.R.C.P.

L. MANDEL, M.B., M.R.C.P.

K. B. TAYLOR, B.M., M.R.C.P.

AND

M. R. JEFFREY, M.B., M.R.C.P.

*(From the South-west and Oxford Regional Rheumatism Research Unit, Royal National Hospital for Rheumatic Diseases, Bath)*

We have previously reported the effects of insulin hypoglycaemia upon rheumatoid arthritis (Kersley *et al.*, 1950). Of 80 patients treated, two developed attacks of spontaneous hypoglycaemia shortly after therapy ended. This complication is not mentioned by Sargant and Slater (1948) in discussing the use of hypoglycaemic therapy in mental disease. Our two cases were therefore thought to be worthy of a brief report.

## Case 1

A married woman aged 36 had a four-months history of rheumatoid arthritis affecting the hands, feet, and knees. Her general health was quite good. No special treatment had been given. She had had rheumatic fever at 32. Her mother and two uncles have rheumatoid arthritis.

On examination grip was poor in both hands, and there was swelling and tenderness of all proximal interphalangeal joints, with slight limitation of movement at the right wrist and pain on passive flexion of the toes. General clinical examination otherwise showed no abnormality, apart from a blowing apical systolic murmur without cardiac enlargement. Her weight was 118 lb (53.5 kg.); E.S.R. 44 mm. in one hour (Westergren); haemoglobin 49%; fasting blood sugar 105 mg. per 100 ml.

### Insulin Therapy

Insulin therapy was given for 13 days, and hypoglycaemic reactions occurred on 10 days with doses of 24 to 38 units of soluble insulin. After treatment her general health was much improved and pain and stiffness in the joints were considerably reduced. The haemoglobin and E.S.R. levels were virtually unchanged. Her weight had risen by 6 lb. (2.7 kg.). The fasting blood sugar one week after the end of treatment was 100 mg. per 100 ml. The improvement lasted for about five weeks, but after a further month the condition had relapsed to a state slightly worse than before treatment.

Three months after the end of the first course a second course of hypoglycaemia was given, lasting five days, on four of which good reactions occurred with doses of 32 to 44 units of insulin. Some improvement in joint pain and stiffness resulted, though this was less than on the previous occasion. It was hoped to maintain this improvement by giving single weekly hypoglycaemic reactions. Therefore one week after the end of the second course 36 units of insulin was given but no reaction followed. One week later (August 9, 1950) she reported again, but insulin was not given, as she had had diarrhoea and nausea for four days. She returned home and the diarrhoea settled in two to three days. On August 14 she had a slight pyrexia of undetermined cause.

On August 15, 12 days after the last dose of insulin, the patient's husband awoke at about 3 a.m. to find her sitting up in bed in a delirious condition, which lasted four hours and was followed by spontaneous sleep. The patient had no memory of the attack, and appeared normal when seen by her doctor at 11 a.m. Attacks occurred daily until her admission on August 19, but appeared a little later each successive day and became less severe. On August 20 an attack, characterized by vertigo, blurred vision, weakness of the limbs, sweating, and shivering, started at 7.20 a.m. After 6 oz. (170 g.) of glucose by mouth she rapidly recovered. On August 21 she had mild diplopia and right-sided weakness at about 9.30 a.m., when the fasting blood sugar was found to be 23 mg. per 100 ml. Mild attacks occurred before breakfast on August 22, 23, and 24. A high-protein diet was then given and a milk drink at 10 o'clock each night. No further attacks occurred, and the patient was discharged on August 29.

### Investigations

On August 22, 19 days after the conclusion of insulin treatment and seven days after the first attack of spontaneous hypoglycaemia, the glucose-tolerance curve showed:

| | | | |
|---|---|---|---|
| 9 a.m. (fasting) | blood sugar | .. | = 40 mg. per 100 ml. |
| 50 g. of glucose given | | | |
| After ½ hour | blood sugar | .. | = 40 „ „ „ „ |
| „ 1 hour | „ „ | .. | = 66 „ „ „ „ |
| „ 2 hours | „ „ | .. | =166 „ „ „ „ |
| „ 3 hours | „ „ | .. | = 71 „ „ „ „ |

No glycosuria occurred.

*9 a.m.:* Plasma alkaline phosphatase, 2 units; plasma bilirubin, less than 0.2 mg. per 100 ml.; serum colloidal gold reaction, 3; thymol turbidity, 2.5 units; serum potassium, 15 mg. per 100 ml.; blood urea, 28 mg. per 100 ml.; eosinophils (direct count), 55 per c.mm. *12 noon:* Eosinophils, 0. *2 p.m.:* Eosinophils, 28 per c.mm.; serum potassium, 17.3 mg. per 100 ml.

## Case 2

A woman aged 43 had a 12-years history of slowly progressive rheumatoid arthritis; most joints were involved. Her general health was fair. She had had physiotherapy but no gold.

Examination showed her to be frail, her weight being 78 lb. (35.4 kg.). The mucosae were pale. There were marked rheumatoid changes in hands, feet, ankles, wrists, elbows, shoulders, and knees. No abnormality was found in the heart, lungs, abdomen, or C.N.S. The E.S.R. was 59 mm. in one hour (Westergren); haemoglobin 58%; fasting blood sugar 100 mg. per 100 ml.

### Insulin Therapy

Insulin therapy was given for 20 days, hypoglycaemic reactions occurring on 15 days with doses of 20 to 38 units of insulin. On the day when the latter dose was given treatment had to be interrupted by administering intravenous glucose because of the onset of coma.

After treatment there was some improvement in her general health, and her weight had risen by 5 lb. (2.3 kg.). The joints were generally less painful and stiff, but there was no objective change on examination. Three days after the end of treatment the fasting blood sugar was 50 mg. per 100 ml.; E.S.R. 70 mm. in one hour; haemoglobin 67%. The subjective improvement lasted about two months, and then relapse occurred to a state slightly worse than before insulin therapy.

Four months after the first, a second course of insulin was given, lasting 13 days, on seven of which a good reaction occurred. This course again produced some subjective improvement but no objective change. On November 10, 1950, the day after the last insulin treatment, the patient was found to be sweating and incoherent at 6 a.m., and was later incontinent of urine. She revived after oral glucose was given. On November 12 a similar attack took place and was again terminated by oral glucose. In this second attack the blood sugar was 38 mg. per 100 ml. Only one further attack occurred, 10 days later at 1 p.m. after an overnight fast and towards the end of a hippuric-acid test.

It later transpired that this lady usually took a milky drink at 9.30 p.m.; on both the evenings preceding the hypoglycaemic attacks she had not taken this drink.

### Investigations

The last insulin treatment was given on November 9, and spontaneous hypoglycaemic attacks occurred on November 10, 11, and 12.

*November 10–11.*—Total neutral 17-ketosteroids, 6.2 mg. per 24 hours; cortins, 2 mg. per 24 hours.

*November 11.*—Glucose-tolerance curve:

| | |
|---|---|
| Fasting blood sugar .. .. | = 74 mg. per 100 ml. |
| 50 g. of glucose given | |
| After ½ hour blood sugar .. | =125 „ „ „ „ |
| „ 1 „ „ „ .. | =142 „ „ „ „ |
| „ 1½ hours „ „ .. | =166 „ „ „ „ |

Unfortunately no further specimens were taken.

*November 11–12.*—Total neutral 17-ketosteroids, 5.4 mg. per 24 hours; cortins, 1.75 mg. per 24 hours.

*November 13.*—Insulin-sensitivity test:

| | |
|---|---|
| Fasting blood sugar .. .. | = 23 mg. per 100 ml. |
| 5 units of soluble insulin given intravenously | |
| After 20 mins. blood sugar .. | = 27 mg. per 100 ml. |
| „ 30 „ „ „ .. | = 23 „ „ „ „ |
| „ 45 „ „ „ .. | = 40 „ „ „ „ |
| „ 60 „ „ „ .. | = 43 „ „ „ „ |
| „ 90 „ „ „ .. | = 40 „ „ „ „ |
| „ 120 „ „ „ .. | = 31 „ „ „ „ |
| Adrenaline hydrochloride given, 0.4 mg. intramuscularly | |
| After 45 mins. blood sugar .. | = 33 mg. per 100 ml. |
| „ 60 „ „ „ .. | = 31 „ „ „ „ |

*November 14.*—Glucose-tolerance test:

| | |
|---|---|
| Fasting blood sugar .. .. | = 44 mg. per 100 ml. |
| 50 g. of glucose given | |
| After ½ hour blood sugar .. | = 91 „ „ „ „ |
| „ 1 „ „ „ .. | =105 „ „ „ „ |
| „ 2 hours „ „ .. | =111 „ „ „ „ |
| „ 3 „ „ „ .. | = 64 „ „ „ „ |
| „ 4 „ „ „ .. | = 25 „ „ „ „ |

*November 15.*—A.C.T.H. test: eosinophils, 9 a.m., 70 per c.mm.; 25 mg. of A.C.T.H. given intramuscularly; eosinophils, 1 p.m., 36 per c.mm.

*November 16.*—Control eosinophils: 9 a.m., 56 per c.mm.; 1 p.m., 95 per c.mm. Total neutral 17-ketosteroids, 8.7 mg. per 24 hours; cortins, 1.9 mg. per 24 hours.

*November 23.*—Oral hippuric acid synthesis test: 4 g. of sodium benzoate given; three hourly specimens of urine secured; the fourth hourly specimen could not be collected owing to a hypoglycaemic attack. In the three-hours urine collection (volume 900 ml.) 2.84 g. of sodium benzoate was excreted as hippuric acid.

*November 24.*—Insulin-sensitivity test:

| | |
|---|---|
| Fasting blood sugar .. .. | = 47 mg. per 100 ml. |
| 5 units of insulin given intravenously | |
| After 20 mins. blood sugar .. | = 22 mg. per 100 ml. |
| „ 30 „ „ „ .. | = 58 „ „ „ „ |
| „ 45 „ „ „ .. | = 58 „ „ „ „ |
| „ 60 „ „ „ .. | = 58 „ „ „ „ |
| „ 90 „ „ „ .. | = 47 „ „ „ „ |
| „ 120 „ „ „ .. | = 41 „ „ „ „ |
| 0.4 mg. of adrenaline hydrochloride given | |
| After 45 mins. blood sugar .. | = 41 „ „ „ „ |
| „ 60 „ „ „ .. | = 33 „ „ „ „ |

*November 28.*—Oral galactose-tolerance test: 7.3 g. of galactose excreted in five hours after dose of 40 g.

*November 29.*—Laevulose-tolerance test: fasting blood sugar, 74 mg. per 100 ml.; blood sugar, one hour after test, 116 mg. per 100 ml.

*December 7.*—Fasting blood sugar, 80 mg. per 100 ml.

*December 9.*—Fasting blood sugar, 100 mg. per 100 ml.

*December 11.*—Glucose-tolerance test:

| | |
|---|---|
| Fasting blood sugar .. .. | = 95 mg. per 100 ml. |
| 50 g. of glucose given | |
| After ½ hour blood sugar .. | =190 „ „ „ „ |
| „ 1 „ „ „ .. | =200 „ „ „ „ |
| „ 2 hours „ „ .. | =142 „ „ „ „ |
| „ 3 „ „ „ .. | = 54 „ „ „ „ |

### Six Other Cases

In view of the occurrence of these two cases of spontaneous hypoglycaemia, six cases of rheumatoid arthritis which had received courses of insulin hypoglycaemia had daily blood-sugar estimations carried out for 10 days after cessation of treatment. The results of these tests are plotted in the accompanying Chart. In three cases

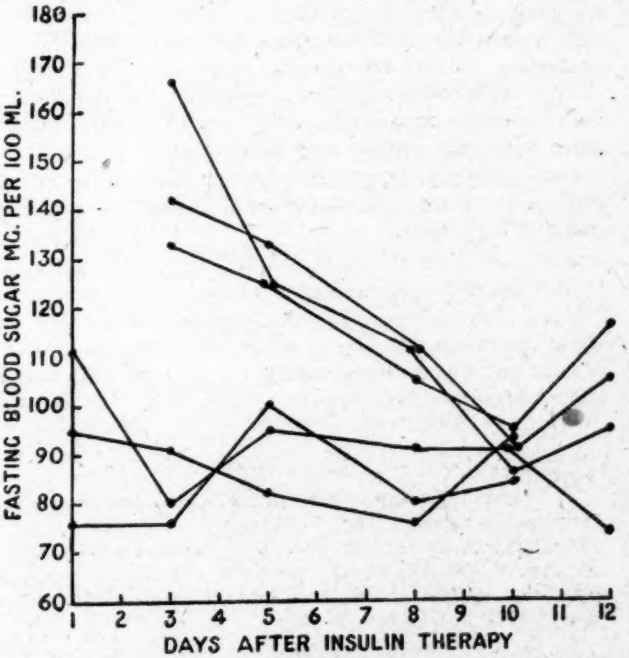


Chart showing changes in fasting blood-sugar levels in six cases following insulin treatment.

there was a tendency to initial fasting hypoglycaemia followed by a drop in blood sugar, maximal about the tenth day, and then a rapid return to normal values.

### Comment

The occurrence of frank attacks of spontaneous hypoglycaemia after insulin therapy is not common; these two cases are the only examples seen in the 80 cases of

rheumatoid arthritis to which we have now given insulin. It may be significant that in both cases the attacks followed a second course of insulin: we have now given second courses to 12 patients.

In Case 1 the attacks did not begin until 12 days after the last insulin treatment, the patient having suffered meanwhile from gastro-enteritis. The investigations done when she was readmitted did not elucidate the mechanism of the hypoglycaemia. It may be noted, however, that the glucose-tolerance curve suggested slow absorption; that the adrenal response to hypoglycaemia, as judged by subsequent eosinophil depression, was normal; and that the serum colloidal gold reaction was positive (3), thymol turbidity, alkaline phosphatase, and plasma bilirubin being normal.

In Case 2 the spontaneous hypoglycaemic attacks started on the day after the last insulin treatment and must be wholly attributed to the therapy. Evidence of undue sensitivity to the hypoglycaemic action of insulin was sought three days after the first spontaneous attack. In fact, five units intravenously produced no depression at all of the very low fasting blood sugar; neither did adrenaline, given later, produce any rise. Glucose tolerance on the following day was apparently normal, though the curve was pitched at a low level owing to the subnormal fasting blood sugar. One day later 25 mg. of A.C.T.H. produced normal depression of circulating eosinophils.

Several liver-function tests were done between 10 and 15 days after the first spontaneous attack. The oral hippuric-acid synthesis test was probably normal, laevulose tolerance was at the outside limit of normal, and galactose tolerance was distinctly abnormal. A second insulin-sensitivity test was also done at this time. This showed a normal blood-sugar depression 20 minutes after 5 units of insulin intravenously; the depression had, however, been abolished 10 minutes later. Adrenaline was again without any effect at all.

One month after the first attack the fasting blood sugar was normal and the glucose-tolerance curve was of the "lag" type.

From the clinical aspect, the attacks were easily controlled by the institution of a high-protein diet with a "snack" at bedtime. It would seem wise to insist on these measures for three weeks after any course of insulin therapy, for the attacks, though not serious, are distressing to patients and their relations.

**Summary**

Two cases of rheumatoid arthritis developed attacks of spontaneous hypoglycaemia in the early morning shortly after the end of second courses of insulin hypoglycaemic therapy. The attacks were controlled by a high-protein diet with a feed at bedtime, and the tendency to them disappeared within two weeks.

In six other patients who had received similar treatment, daily fasting blood-sugar estimations for 12 days after stopping insulin administration showed that the lowest blood sugars occurred about the tenth day.

We would like to express our appreciation to Dr. H. J. Gibson and his laboratory staff for some of the pathological investigations, and to Dr. P. Woolf for assistance.

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# THE NEUROLOGICAL ORIGIN OF PEPTIC ULCER

## FRONTAL-LOBE LESIONS AND GASTRIC ULCER

BY

**J. L. ARTETA, M.D.**

*Pathologist, Institute of Medical Pathology, Madrid*

There are many reasons, mainly experimental, for belief in the existence of a cortical relation to visceral sensitivity. As Fulton (1943) has said, in the vegetative nervous system, just as in the somatic nervous system, there exist suprasegmental levels capable of influencing intersegmental autonomic reflexes.

The work of Watts and Fulton (1934) and of Davey (1949) has shown the existence of areas in the cerebral cortex whose stimulation or ablation causes changes in the behaviour of the gastro-intestinal tract. These changes are in the motility and secretions of the stomach and intestinal tract.

Cortical relationship to the alimentary tract is confined to the frontal lobes. Stimulation of the sixth area of the frontal lobes in monkeys (Watts and Fulton, 1934) has resulted in an increase of intestinal peristalsis to the extent of obstruction due to intussusception. Davey (1949) obtained similar results with operations on this area, but according to him it is the ocular region of the cortex which reacts best, producing more active changes in the behaviour of the stomach and intestines.

Anatomical evidence has also furnished further proof of these facts. Gastric or intestinal ulceration is often found in experimental animals subjected to cerebral operations. Mettler *et al.* (1936) frequently found gastro-intestinal ulceration in decorticated animals. The earliest account in the literature is that of Brown-Séquard (1876), who reported a perforated gastric ulcer in a dog whose frontal lobes he had cauterized.

There is plenty of clinical evidence to support the relation between the cerebral cortex and the digestive tract. It is well known that in some subjects strong emotions can produce intestinal disturbances due to disorders of motility; the alimentary character of the aura of some epileptic attacks; and the digestive disturbances, usually intestinal, which occasionally occur in leucotomy cases. Among the most significant observations on this subject is a case described by Cushing (1932). Despite the fact that he maintained the view that in those cases in which the gastric lesion had a neurological origin this was to be referred to the hypothalamus, as it is here that vegetative functions are represented and integrated, his case may well be cited. In Cushing's case there were found at post-mortem examination multiple superficial bleeding ulcers in the stomach and duodenum, and in the brain the remainder of a meningioma, previously removed, situated in the olfactory groove, together with a large area of softening in the frontal lobe caused by ligation of the anterior communicating cerebral artery.

Bodechtel (1935) in one of his cases found a glioblastoma multiforme of the frontal lobe and multiple acute bleeding ulcers of the stomach.

I have been able to study post mortem two cases of frontal-lobe lesions associated with multiple acute ulcerations in the stomach and duodenum that may be

brought forward as further proof of the relation between the cerebral cortex and the digestive tract.

### Case 1

A 25-year-old man came to necropsy with the diagnosis of pneumococcal meningitis bacteriologically confirmed. There was a purulent meningitis localized to the frontal region. Both frontal lobes were completely covered by a creamy exudate, greenish-yellow in colour, which spread over the anterior half of the brain and filled the sulci (Fig. 1, A). The rest of the brain was quite free of exudate. In addition to the purulent exudate there was a circular depression (shown in the photograph) with well-marked borders which was surrounded by an indefinite area of dull colour, dark blue in the fresh specimen. On section this was seen to be due to a haemorrhage in the anterior portion of the frontal lobe. The stomach contained a little dark-brown fluid and "coffee-ground" material, and in the duodenum immediately beyond the pylorus there were seven ulcers (Fig. 2). These varied in size, and had well-defined edges and dark bleeding bases. Some were very superficial, merely erosions, others deeper and funnel-shaped. There were no other important findings.

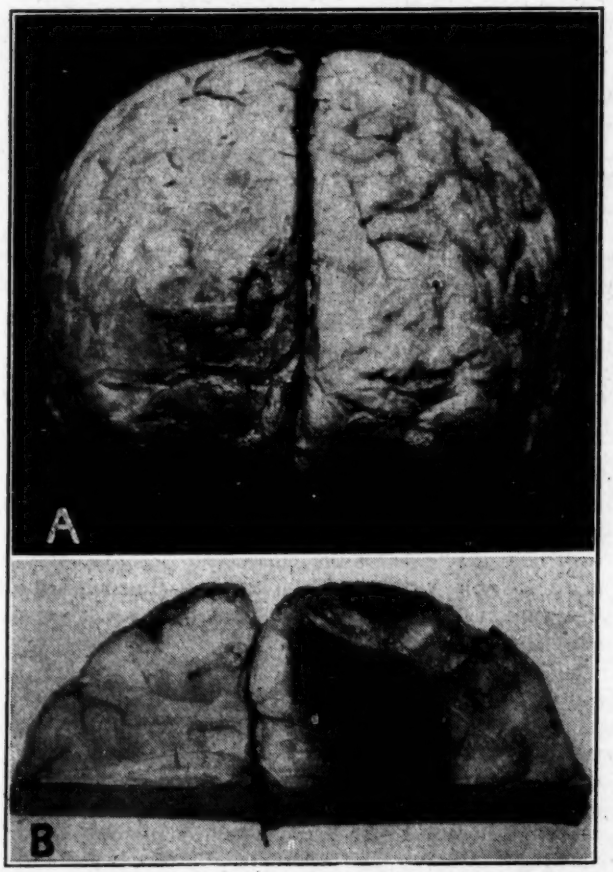


FIG. 1.—Case 1. A, Frontal lobes covered by exudate. B, Section showing circular depression and haemorrhage.

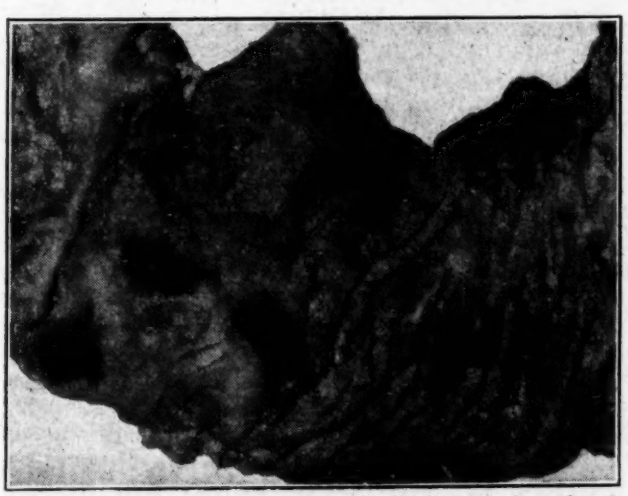

FIG. 2.—Case 1. Duodenum immediately beyond the pylorus, showing seven ulcers.

### Case 2

A man aged 35 died with signs of a haemorrhage into a cerebral frontal tumour. There was no history of digestive trouble. Necropsy revealed swelling of the anterior half of the left cerebral hemisphere with well-marked signs of raised intracranial pressure and marked flattening of the convolutions. The brain was hardened, and on subsequent section the whole of the left frontal lobe was seen to be invaded by a tumour, in the centre of which were several areas of haemorrhage, softening, and necrosis (Fig. 3). The tumour filled the whole of the frontal lobe and obliterated the anterior horn of the ventricle, which was represented by a small groove towards the posterior end of the tumour. The lateral ventricle and frontal lobe on the right side were deformed and displaced by the tumour. There was also displacement of the caudate and lenticular nuclei, both limbs of the internal capsule, and the optic thalamus on the left side. There were haemorrhages into the lenticular nucleus and the thalamus on this side, and there was hydrocephalus, all of which is well shown in Fig. 3. The tumour was proved to be an ependymoma, using the silver carbonate method of Rio-Hortega.

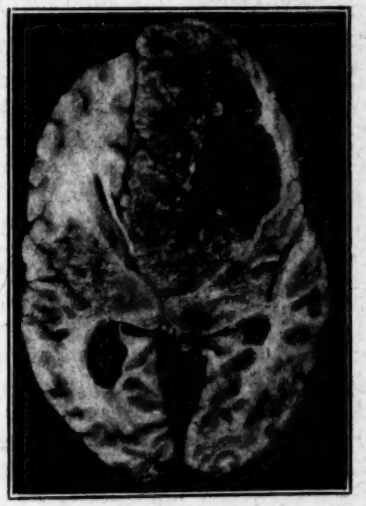

FIG. 3.—Case 2. Showing left frontal-lobe tumour in the centre of which are several areas of haemorrhage, softening, and necrosis.

In the stomach there were four ulcers very similar to those in the previous case (Fig. 4). It should be pointed out that these ulcers were situated in the upper part of the greater

FIG. 4.—Case 2. Showing four stomach ulcers.

curvature and not on the line of the lesser curvature, as is the rule in chronic gastric ulceration. The stomach contents consisted of the typical coffee-ground fluid with some supernatant small clots of blood.

From their shape, their number, and their bleeding character we may accept these as acute ulcers similar to those in the previous case, and more especially as there was in Case 2 no history of any previous subjective or objective gastric disturbance.

### Discussion

These two cases demonstrate the close relationship between gastric ulceration and localized lesions of the cerebral frontal lobe.

The nature of the ulceration does not correspond to that of the chronic gastric or duodenal ulcer. The haemorrhagic character, number, site, and funnel shape of these ulcers are typical of acute ulcers due to haemorrhage. The primary cause is a local vascular disturbance, possibly related to alteration of the gastric motility, which produces haemorrhages that separate the epithelium from the submucosa. The devitalized epithelium is then digested away by the gastric juice and a superficial erosion produced. The funnel shape and the depth of some of these ulcers are, similarly, evidence of their vascular origin.

The regulating action of the cerebral cortex—in particular certain areas of the frontal lobe—has been firmly established experimentally, so that in these two cases we may accept the evident relationship between the cerebral lesions and the gastric and intestinal changes.

As for the anatomical pathways which take part in the transmission of regulating impulses from the cortex, at present three are accepted as connecting the frontal area to the primary subcortical centres—one to the anterior thalamic nucleus, another to the dorso-medial nucleus of the thalamus, and a third to the hypothalamus, though this latter has no firm anatomical basis, its existence being accepted only through the physiological observations of Ward and McCulloch (1947).

It is possible that in addition to these direct and indirect connecting pathways to the hypothalamus other extrapyramidal tracts may regulate the primary and autonomic centres, as may be deduced from the work of Spiegel and Hunsicker (1936).

### Summary

Two cases of frontal-lobe lesions with acute multiple ulceration of the stomach and duodenum are described.

In one case there was a purulent pneumococcal meningitis localized to the frontal area, together with seven acute ulcers in the duodenum. In the other case there was an ependymoma of the frontal lobe with four acute ulcers in the greater curvature of the stomach.

The possible mechanism in the production of these ulcers is discussed along with their relation to vascular changes and alterations in gastric motility of cerebral origin.

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## THE TREATMENT OF BLEPHARITIS

BY

**D. AINSLIE, F.R.C.S.**

*(From the Institute of Ophthalmology, London. Director of Research, Sir Stewart Duke-Elder)*

Blepharitis, though sometimes dismissed lightly as a minor complaint, is in fact one of the most distressing afflictions met with in ophthalmic practice. Even with the wide range of antibacterial substances now available some cases prove very obstinate, causing prolonged suffering to the patient. The majority can be cured, however, if appropriate antiseptics or antibiotics are used before the disease has become chronic.

The mildest form—squamous blepharitis, manifests itself by a scaliness of the lid margins. It is merely dandruff of the eyelashes, associated with seborrhoea elsewhere. Dandruff of the scalp is an almost constant accompaniment. Squamous blepharitis is itself not serious except in so far as, if neglected, it is likely to pass on to the more severe condition of ulcerative blepharitis in which pyogenic infection of the skin of the lid margins has supervened. Shallow ulcers then form near the bases of the lashes and become covered by a thick yellow crust. By far the commonest infecting organism is *Staphylococcus aureus*, but any pyogenic organism may be found.

Ulcerative blepharitis is serious, for if not cured at an early stage it will become chronic and lead to a deep folliculitis. After this has happened even the most assiduous treatment may fail to eradicate the infection, and scarring of the lid margins with trichiasis, epiphora, and dermatitis of the surrounding tissues will ensue. It is important, therefore, that the action of the different classes of antibiotic and antiseptic substances should be understood so that each may be used to best advantage.

### Treatment

As with any inflammatory lesion, the results of local treatment will be disappointing if general measures are not employed when necessary. Particularly in the case of children is it found that sufferers from ulcerative blepharitis are debilitated. A holiday in the fresh air, good food, and preparations containing the vitamin-B complex may be of the greatest value.

An uncorrected error of refraction is often blamed as the cause of blepharitis. While this is never the true cause, the ocular discomfort and asthenopia which result play their part in undermining the general constitution. Refractive errors should therefore be meticulously corrected.

*Squamous Blepharitis.*—As with dandruff of the scalp, the scaliness of the lids in squamous blepharitis is the result of epidermal irritation following infection by pityrosporum. Treatment consists in frequent bathing with a 2% solution of sodium bicarbonate in order to remove the scales, followed by the application of 1%

ung. hydrarg. oxidi flavi or 1% ung. hydrarg. ammon. dil. While this will rapidly clear up the lid condition the disease will immediately recur on cessation of treatment unless the seborrhoea of the scalp, and possibly of the eyebrows, is also dealt with. Lotions containing salicylic acid, mercury perchloride, sulphur, or resorcin are the most effective. Persistent treatment, consisting in frequent washing of the hair and applications of the lotion, will clear the dandruff, but periodic treatment should be continued indefinitely, as recurrences, usually due to reinfection, are common.

*Ulcerative Blepharitis.*—The successful treatment of ulcerative blepharitis is more difficult, but resolves itself into the removal of the encrustations by mechanical means and the application of an antiseptic preparation to the infected parts thus exposed.

## Methods of Treatment

*Non-specific Antiseptics.*—Until quite recently non-specific antiseptic ointments were the only means of treatment, and they are still of great value. Sodium bicarbonate 2% is at first used to soften and remove the crusts, and 1% (or 2%) ung. hydrarg. oxidi flavi is then rubbed firmly into the raw areas. This should be repeated three or four times daily. After the first few days a change from sodium bicarbonate to oxycyanide of mercury lotion 1:8,000 can be made with benefit, as this is a powerful antiseptic in itself and is useful in combating any associated conjunctivitis. The importance of removal of the crusts cannot be too strongly emphasized. No matter what ointment is used, it will be useless if held away from the infected area by a barrier of encrustation.

*Sulphonamides.*—Since the introduction of the sulphonamides drugs of this class have often been employed, and the popular sulphacetamide, as a 6 to 10% ointment, has been used in thousands of cases. I have found it effective in some instances, and it has the merit of being a perfectly safe preparation, allergic responses being of the utmost rarity. I have not, however, found the results superior to those obtained with yellow oxide of mercury. Whatever the situation when sulphacetamide was first introduced, it is now certain that in many cases organisms are resistant to the drug.

*Penicillin.*—With the discovery of penicillin the era of antibiotics became established. Penicillin, with its great potency as an antibiotic against the coccal organisms, was found to be a most useful agent in the treatment of blepharitis. The application of penicillin ointment led to rapid, and in many cases complete, cures. Unfortunately, however, penicillin has been used somewhat indiscriminately, all too often in inadequate amounts. Some strains of staphyloccoci have always been penicillin-resistant, but now poorly sensitive and insensitive strains are becoming more frequent. It is unfortunate that, while the staphylococci have managed to become more resistant, the human subject is becoming more sensitive to penicillin, and allergic responses, once rare, are now common. If the use of penicillin, or for that matter any antibiotic, is under consideration, the likelihood of a cure must be weighed against the danger of allergy. There is undoubtedly a place for the use of penicillin ointment in the treatment of blepharitis, but I do not believe that it should be used empirically without a culture and, if possible, a test of the organism's sensitivity. If this precaution is not taken the patient may be unnecessarily exposed to the risk of an allergic response, with the unpleasant eczematous reaction and, indeed, possibly secondary dermatitis. If penicillin is used without cultural control it should certainly not be persisted with for more than a few days in the face of anything but the most rapid improvement. The most useful penicillin preparation in the treatment of blepharitis is an ointment containing 25,000 units per gramme.

*"Aureomycin."*—Recently other antibiotics have become available. Aureomycin, with its wide range of antibiotic activity, covering the cocci, most Gram-negative bacilli, and even some of the larger viruses, suggested attractive possibilities. Through the kindness of surgeons of the Moorfields, Westminster, and Central Eye Hospital I have had the opportunity of testing the effectiveness of aureomycin in a variety of ophthalmic infections, including a number of cases of blepharitis. Here it held out especially bright prospects, as staphylococci which have become resistant to penicillin are still in most cases susceptible to aureomycin.

## Results of Treatment with Aureomycin

As aureomycin is soon likely to be generally available I am recording the results obtained in the treatment of 30 consecutive cases of blepharitis. All the cases were well established, and the blepharitis had been present for periods varying from three months to over twenty years. In view of this and the fact that all had had numerous previous treatments, including mercurial ointments, application of silver salts, sulphonamides, and penicillin, the results have been encouraging. A number of long-standing cases, including one of twenty-six years' duration, have been brought under control and have remained clear for over six months. It will be noted, however, that, even as the result of vigorous treatment with aureomycin, cures for three months or more have been possible in only two-thirds of the cases. This, I think, emphasizes the importance of thorough treatment while the disease is yet in an early stage.

In each of the 30 cases a culture was taken, the results of which are shown in Table I. *In vitro* sensitivity of the organism to penicillin and aureomycin was tested in all cases with positive culture. Twelve were tested against sulphacetamide ("albucid.") Testing was purely qualitative, it being observed whether or not the growth of the organism in question was inhibited by the various therapeutic preparations—that is, a penicillin, sulphacetamide, or aureomycin solution. Very slight inhibition was regarded as negative.

TABLE I.—*Results of Culture and Sensitivity of Organisms in vitro*

| Organism Grown | No. of Cases | Penicillin-Sensitive | Sulphacetamide-Sensitive | Aureomycin-Sensitive |
|---|---|---|---|---|
| *Staph. aureus* .. | 22e | 11 | 4 (12 tested) | 21 |
| *B. friedlanderi* .. | 3 | 0 | 2 | 3 |
| No growth .. | 5 | — | — | — |

The paper-disk method of testing for sensitivity was employed. Pieces of filter-paper 7 mm. in diameter were soaked in the various solutions and placed on the blood-agar plate upon which the organism under test was growing. The strength of solution in the case of penicillin was 500 units per ml., aureomycin 1 mg. per ml., sulphacetamide 30%.

Table I shows that the overwhelming majority of cases were due to *Staph. aureus*, and it will be seen that

a high proportion of these were insensitive to penicillin and sulphacetamide. This in no way gives a representative picture of the general sensitivity of organisms in blepharitis, for the cases were selected because they had failed to respond to ordinary treatments. The percentage of penicillin- and sulphacetamide-insensitive causative organisms is certainly much higher than average.

The results of treatment with aureomycin are given in Table II. The cases designated as successful cleared up

TABLE II.—*Results of Aureomycin Treatment*

| Culture Result | No. | Successful | Unsuccessful | |
|---|---|---|---|---|
| | | | Recurred | Did not Improve |
| *Staph. aureus* .. | 22 | 13 | 6 | 3 |
| *B. friedlanderi* .. | 3 | 3 | 0 | 0 |
| No growth .. | 5 | 2 | 0 | 3 |
| Total .. | 30 | 18 | 6 | 6 |

as the result of a single course of treatment and have remained clear for from three to twelve months. The unsuccessful cases either failed to improve or recurred soon after cessation of treatment. Two recurrent cases responded well to a second course and have now remained clear for over two months.

Treatment of these cases was as follows: the crusts were removed with warm saline solution and aureomycin ointment was applied to the ulcerated areas. The patient was instructed to apply the ointment every two hours during the day, and the importance of removing any crusts which had re-formed was emphasized. After three to four days the ointment was applied four-hourly. In every successful case there was a marked improvement during the first week and the lids appeared to be cured within two to three weeks. Treatment was continued for total periods of five to six weeks, however, in order to minimize the risk of recurrence.

All the successful cases were treated by local application only. Those with a marked associated conjunctivitis were, in addition to the ointment, given aureomycin drops every three hours for three days. The cases which did not respond to these measures were also given systemic aureomycin (orally, 500–750 mg. every six hours) but without improvement. It would appear, therefore, that an intensive course of local treatment is the correct method of approach, and that if this is ineffective systemic administration is likely to be equally useless.

The ointment used was the standard preparation of the American Cyanamid Company (Lederle Division) and contained 1 mg. of crystalline aureomycin per gramme. This is a stable preparation remaining active without refrigeration for over a year.

Drops were freshly made up before use, as in solution aureomycin deteriorates rapidly. Lederle prepared a dry powder containing aureomycin hydrochloride 25 mg., sodium borate 25 mg., and sodium chloride 62.5 mg.; and 5 ml. of distilled water is added. In this way 0.5% solution of aureomycin, suitably buffered, is obtained.

### "Terramycin"

During the past few weeks I have been fortunate in having available terramycin, in the form both of ophthalmic drops 0.5% and of ophthalmic ointment 0.1%, supplied by Chas. Pfizer, of New York. As with aureomycin, the drops must be freshly made up, and a suitable dry powder is supplied by Pfizer. The ointment is stable.

I have treated only two cases of blepharitis with terramycin and in each case ointment alone has been employed. In both, cultures revealed *Staph. aureus*, and in both the organism was insensitive to sulphacetamide and penicillin but sensitive to aureomycin and terramycin. Improvement with terramycin was immediate. It is, of course, too early to say whether the results are permanent.

### Conclusion

In view of the number of antibacterial substances now available the best results will be obtained only if an orderly line of treatment is followed. The danger of allergic responses and the danger of producing insensitive organisms make it desirable to reserve antibiotics for cases failing to respond to older treatments. Empirical remedies, such as mercurial ointments, are very often effective, but if, after a reasonable trial, there is little or no relief a culture and a sensitivity test should be performed so that the most appropriate antibiotic can be chosen. In this way prolonged ineffective treatment will be avoided and the danger of allergic responses minimized. Once treatment with an antibiotic is decided upon it must be conducted with the utmost vigour so that the danger of producing insensitive strains of the organism will be reduced to a minimum.

### Summary

The results of treatment with aureomycin of 30 cases of long-standing blepharitis are given.

The initial results in two cases treated with terramycin are mentioned.

A line of treatment for blepharitis is suggested.

I should like to thank Dr. N. H. Ashton and his staff in the pathological department of the Institute of Ophthalmology for performing so many cultures and sensitivity tests.

# Medical Memoranda

## Metastatic Adrenomedulloblastoma of the Pterygopalatine Fossa

It will be recalled that neuroblastoma of the right adrenal medulla tends to metastasize to the retroperitoneal glands, liver, and lungs, producing Pepper's syndrome (Pepper, 1901), whereas neuroblastoma of the left adrenal medulla usually metastasizes to the cranium and long bones, producing Hutchison's syndrome (Hutchison, 1907). It is with the latter that we are concerned in this brief contribution, although the two classical types tend to merge into one another, owing to the intense malignancy of the tumour.

Adrenal, mesencephalic, and retinal neuroblastomas all arise from undifferentiated neural elements. They are highly cellular, and the cells are small and dark, tending to become arranged in pseudo-rosettes.

### Case Report

A baby girl aged 8 months was referred by Dr. Kenneth Dick to the E.N.T. Department of the Royal Halifax Infirmary because of a swelling in the right temporal region of three weeks' duration. There was no evidence of otitis media. The eyelids were slightly discoloured, but our ophthalmic colleague, Mr. P. M. Wood, reported that the media and fundi were normal. The temperature varied from 99

to 100° F. (37.2 to 37.8° C.). The blood count was: red cells, 4,520,000; white cells, 18,900 (neutrophil polymorphs 66%, basophils 1%, lymphocytes 32%, large monocytes 1%); haemoglobin, 74%; colour index, 0.8.

During the first week's in-patient treatment the temporal swelling increased and proptosis developed; the infant became increasingly pale, the haemoglobin eventually falling to 18%. As the most careful examination of the abdomen by medical and surgical members of our staff failed to reveal any abdominal tumour, Dr. Chester Williams's offer of deep *x*-ray treatment of the temporal swelling was accepted, but deterioration was inexorable. Eventually a nodular mass became palpable beneath the left costal margin; this gradually filled the abdomen and the legs became swollen. Death occurred on the twenty-second day after admission.

On post-mortem examination by Dr. F. E. Aaron a large tumour of the left suprarenal gland was found to have spread extensively, invading the ovaries. The left kidney was engulfed but not infiltrated, and the liver spared. There were several metastases in the cranium, particularly in the right pterygopalatine and infratemporal fossae and in the brain. Histologically, the tumour consisted of small round cells, with occasional pseudo-rosette formation, typical of neuroblastoma.

### Comment

With regard to differential diagnosis, scurvy was mentioned by Hutchison in his original description of the syndrome. Blood examination will eliminate chloroma and the leukaemias. Splenic puncture may be carried out if Gaucher's disease is suspected. Sternal puncture and the test for Bence-Jones proteosuria are more likely to be called for in adults, but it is always a golden rule to have the entire skeleton *x*-rayed and not just the skull, to exclude multiple myelomatosis and also Hand–Schüller–Christian's disease. Eventually, as has been shown above, abdominal palpation confirms the diagnosis.

W. O. LODGE, M.D., F.R.C.S.Ed., F.I.C.S.,
Otolaryngological Consultant.

M. BROOKES, B.M., B.Ch.,
Registrar.

Halifax and Huddersfield Royal Infirmaries.

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## Spontaneous Rupture of an Angular Pregnancy

The term "spontaneous rupture of the uterus" seems to vary in meaning from writer to writer. A fairly obvious use of the term would be for rupture occurring as the result of some primary defect in the uterus and in no way the result of external causes such as a contracted pelvis, trauma of any sort, or scarring from previous operation. The following case occurred in a woman who was not in labour and whose infant was dead *in utero* before rupture occurred.

### Case Report

A middle-aged Mkamba woman was admitted to hospital on March 17, 1949, having had pain in the epigastrium and vomiting associated with pain in the lower abdomen for the previous 10 days. She stated that she was nine months pregnant, but that the pain was not like labour pains. She had had three normal pregnancies and deliveries; two of the children, the second and the third, were alive. When already three months pregnant she had had some abdominal pain and slight vaginal blood loss for three to four days. She had had recurrent pain ever since.

Examination of the abdomen showed a tumour, presumed to be the uterus, rising 9 in. (23 cm.) above the symphysis pubis in the midline. It was narrower and much firmer than a normal pregnant uterus. Contractions were not felt, foetal parts could not be identified, and the foetal heart could not be heard. Laboratory examinations revealed no abnormality in the urine or stools. A radiograph taken at Nairobi on March 25 showed a foetus in a breech position with considerable overlap of the skull bones as in maceration. It was decided that this was a case of death *in utero*, and it was hoped that the foetus would be aborted in a natural way.

On the afternoon of March 31 she started to have a slight vaginal loss and the abdominal pains were intensified, suggesting a miscarriage. The next morning the abdominal pain had increased considerably and the abdomen was very tender. There was still some slight vaginal loss, and it was thought that there might be concealed haemorrhage. By the afternoon the abdomen was rigid and the patient pyrexial; it was then thought she had developed peritonitis due to infection from the dead foetus. A vaginal examination showed a slightly dilated external os which contained a blood clot. It was decided to treat the supposed peritonitis in a conservative manner in the hope that it would be easier to deal with when the abortion was complete; but next day, with the pulse steady between 110 and 120 and the temperature up to 103° F. (39.4° C.), a decision was made to open the abdomen—simply to insert a drain so as to embarrass the impending parturition as little as possible. It was felt that a caesarean section was out of the question.

On opening the peritoneum there was a gush of blood followed by the appearance of a foetal limb. Further exploration showed a macerated foetus extruding from a tear in the left cornu of the uterus above the point of entry of the tube. The foetus was removed and the blood mopped up; a low-grade peritonitis was found involving the lower coils of the intestine and the uterine peritoneum. Hysterectomy was performed, during which operation the cervix was found to be closed. The wound was sutured and a drain inserted into the pelvis through a separate incision. Intravenous saline was given during the later stages of the operation, as blood was not available. Post-operative penicillin was given. The drain was removed after 48 hours.

### Comment

This case would appear to fit into the group of "spontaneous ruptures of the uterus." Riddell and Scholefield (1938) described a similar case which they thought should be included in the group of angular pregnancies as defined by Munro Kerr and Anderson (1934), such a pregnancy originating in the uterine end of the Fallopian tube, developing towards the uterine cavity, and being normally associated with pain and a tendency to abort. In the case described there was no marked tendency to abort, and the foetus continued to develop in the uterine cavity.

The rupture was presumably the result of infection of the dead and macerated foetus. This infection, by spreading to the already thinned out cornu, was sufficient to cause a spontaneous rupture.

I am indebted to Dr. T. F. Anderson, D.M.S., Kenya, for permission to publish this case history.

E. P. RIGBY, M.B., B.S.,
Medical Officer, Kenya Colonial Medical Service.

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## Haematemesis Due to Extrahepatic Portal Obstruction

Approximately 4% of cases of haematemesis are said to be due to portal hypertension (Tanner, 1950), whether this is the result of hepatic cirrhosis or of extrahepatic causes. A remarkable case was reported by Whipple (1949) of a policeman who was injured while attempting to stop a runaway horse, and developed a pseudo-pancreatic cyst which was drained; subsequently dense fibrosis took place in the region of the splenic vein, with resultant obstruction. I recently saw a similar case in which obstruction to the splenic vein was caused by calcified tuberculous glands; it was symptomatically cured by a splenectomy, as was Whipple's case.

### Case Report

A man aged 52 was admitted on November 23, 1949, with a history of having vomited one pint (570 ml.) of dark-red blood at 6 o'clock that morning. The blood was clotted and not "coffee ground." His past history showed that he had had retrosternal pain after meals for two to three years, coming on for two to three days at a time and then clearing up again for periods of up to a month or more. His appetite had been good until the past few days, and there had been no loss of weight or previous haematemesis or melaena.

He was a worried man with very marked generalized neurofibromatosis. Apart from this, no physical abnormality was detected except that possibly the edge of the liver could be felt below the ribs. His B.P. was 170/110, pulse 100, and Hb 75%. Three days after admission he vomited about 1 oz. (28 ml.) of blood, and a further 10 oz. (284 ml.) on the next day, when his Hb was 38% and the R.B.C. numbered 1,800,000. He was given 3 pints (1.7 l.) of blood, which raised the Hb to 52%, but he again vomited about 20 oz. (568 ml.) of blood the next day, when the Hb fell to 42% and a further transfusion was given. During the next two weeks his condition remained stationary, and his Hb rose steadily to 56%, though he vomited small amounts of blood occasionally. Occult blood in the stool was positive +++ all this time. A barium meal showed no abnormality, and on December 14 he was seen by Mr. Peter Martin, who advised a laparotomy.

*Operation.*—Under general anaesthesia (thiopentone, cyclopropane, and curare—Dr. G. M. Kerr) an oesophagoscopy was first performed, but no varices or ulceration in the oesophagus and cardiac end of the stomach were seen. The abdomen was then opened through a right upper paramedian incision; the stomach, pylorus, duodenum, and liver appeared normal. The spleen, however, was two or three times its normal size and the vasa brevia were prominent and distended. A hard mass, thought to be calcified tuberculous glands, in the region of the coeliac axis, was seen to be obstructing the splenic vein, which was markedly dilated. The spleen was therefore mobilized and removed, a procedure not without difficulty owing to its extreme friability. The abdomen was then closed.

The patient made an uneventful recovery and no further haematemesis occurred, nor was melaena again noted. He has now remained well for 20 months after operation.

### Comment

The treatment of extrahepatic portal block naturally depends upon the nature of the obstructing factor, and, as Linton (1949) says, no surgeon should operate on such a case without being prepared to perform some kind of shunting procedure. Splenectomy is not completely satisfactory, as bleeding often occurs subsequently, but, if the splenic vein alone is obstructed and it is certain that the left gastric vein drains direct into the portal vein and not into the splenic vein by an anomalous route, then splenectomy is justifiable and holds out a good chance of permanent cure. This case would appear to satisfy these criteria, and the immediate post-operative course so far has been eminently satisfactory, though insufficient time has yet elapsed to be certain of the permanency of the procedure.

My thanks are due to Mr. Peter Martin for allowing me to publish this case and for help in preparing this report.

W. A. HAMER, F.R.C.S.,
Senior Surgical Registrar, Tilbury and Riverside General Hospital, Essex.

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## Division and Suture of the Portal Vein

The more recent frequency of operations on the portal vein, such as portacaval anastomosis, and about the portal vein, such as excision of the head of the pancreas for carcinoma, lends importance to knowledge concerning obstruction of a temporary nature to this vessel, and to the effectiveness of suture of the vessel after division. Experimentally in dogs it has been shown that clamping of the portal vein leads invariably to death regularly in about one hour, and this seems to be due to loss of the circulating blood of the systemic system to the vast lake of the portal capillary bed. It appears to be safe to obstruct the portal vein for periods up to half an hour, but for periods between half and one hour there occur irreversible changes in the portal territory with eventual death of the subject (Mallet-Guy *et al.*, 1950).

### Case Report

The patient was a deeply jaundiced woman aged 50. During the course of a pancreatico-duodenectomy for carcinoma it was found that the growth, though small and mobile, was infiltrating the junction of the splenic and superior mesenteric veins. The splenic vein was tied and the superior mesenteric vein and portal veins were clamped, and the intervening involved veins were excised. Anastomosis between the superior mesenteric vein and the portal vein was achieved by means of three segmental continuous sutures of fine silk, and the rest of the operation was completed in the usual way. Convalescence was normal and uneventful in the early days, and the bowels were moved on the fourth day. On the tenth day the patient's condition deteriorated and she died on the sixteenth post-operative day.

At post-mortem examination a leak was found at the site of anastomosis between the biliary system and the intestine, with a mild peritonitis; there was a marked degree of bronchopneumonia. The significant point was that the anastomosis between the superior mesenteric vein and the portal vein was patent apart from an insignificant mural thrombus. There was no evidence of mesenteric thrombosis, and the intestine appeared normal macroscopically apart from some dilatation in its proximal part. The liver appeared normal on gross examination, but unfortunately by an error a microscopical examination was not made.

This case is reported in order to demonstrate that anastomosis of the portal vein seems to be a reasonable procedure.

PETER MARTIN, M.Chir.,
Surgeon, Chelmsford Hospital.

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# Reviews

## MEDICINE IN ANTIQUITY

BY

**CHARLES SINGER, D.M., D.Litt., D.Sc., F.R.C.P.**

If an ant from its nest or a bee from its hive be placed in a container, it will rapidly die, even though given ample food and air. The experiment can be easily tried on the desk. Why do they die? It is because these animals are essentially social. To isolate them is, as it were, to remove a vital organ. Descriptions of such a creature's anatomy, its physiology, its psychology, or of all combined are therefore necessarily and literally "abstractions," fragmentations in fact. Ants and bees can exist and can be understood only in their social settings. So with man, one of the most basically social of all creatures. We study human anatomy, but there is in truth no such thing as a human arm or leg. The things we study are dead arms and dead legs, abstractions or fragmentations of the human fabric. Changing a few words, the same is true of functions. They exist, in full, only in the living and complete fabric of the body.

This is an elementary philosophical proposition. Nevertheless it is constantly overlooked because the necessary fragmentation of knowledge which is implicit in our modern mechanical "scientific" civilization no less constantly obscures it. Man is a member of a society, and he can no more be understood apart from his relation to a society than can a limb apart from the living body. There is no such thing as a man alone. Such a creature would be, as Hippocrates is said to have said, "either a beast or a god." Medicine is, of all studies, the most social in its outlook. Henry Sigerist, our leading medical historian, is essentially a social philosopher, and he has therefore never overlooked the essential social basis of human life. He has always emphasized that man is, before all else, a being whose life can be understood only in the framework of the society in which it is set. It is thus not unexpected that this should be the keynote of his great work.[1] All who have any interest in historical or social medicine—and what medical man has not?—must greet with joy this first of the eight volumes of his monumental *History of Medicine*. Nothing on this scale or with this scope has hitherto been attempted.

### Primitive Cultures

This first volume is devoted to what Sigerist calls "Primitive and Archaic Medicine." What is "archaic," what is "primitive"? The former term, as Sigerist shows, is merely a matter of practical convenience. It is not a question of distinguishing between rational and scientific medicine on the one hand and irrational and magical elements on the other. There are "scientific" elements in the thought of ancient Egypt and Mesopotamia, while much magic and even theurgy survive in modern medical practice that claims to be scientific. Science, Sigerist holds, did not begin with the Greeks, though perhaps it was they who elevated science into a "discipline." Therefore it is only as a matter of practical convenience, not of principle, that he closes this volume with the medicine of the ancient empires. Their medicine is "archaic" to us not because it differs fundamentally from Greek or other later medicine but because we are necessarily less familiar with its sources.

The idea of "primitive," on the other hand, though as a word it implies a misconception or fallacy, does correspond to something real. The idea of the primitive contains something very subtle which requires much discussion for its definition or limitation. In the strictest logical sense the Australian "black fellow" is no more "primitive" than we are. His society, like ours, has undergone a long evolutionary course from that of his and our prehuman ancestors. But despite this there is no better word than "primitive" for those human societies that are still in the hunting stage. To the problem of what is primitive Sigerist devotes some pages of extraordinary interest. He gives reasons for holding that "in medicine we certainly can distinguish between primitive and advanced conditions," that "the beginnings of medicine were primitive everywhere and that conditions were similar to those of to-day's primitive peoples," and that "the study of primitive medicine, of primitive culture at large, has very practical significance." The section in this volume on the medicine of primitives is, we believe, the only recent attempt to cover the area and to gather up many widely scattered threads. This must have been in itself a formidable task. The results would be quite adequate for a separate work.

### Egypt and Mesopotamia

The central feature of the volume is that which contains the two extensive sections on ancient Egypt and ancient Mesopotamia. Since the publication of the Edwin Smith papyrus by the late Professor Breasted in 1930, knowledge of Egyptian medicine has advanced rapidly. The progress has been not so much factual as comparative and in the due adjustments of emphases. These advances have been made in a multitude of separate contributions, so that there was great need for a general survey of Egyptian medicine. Such a synoptic view is now available in what is, perhaps, the best section of a very good volume. It has involved an immense amount of study, and the marshalling of the scattered material is truly masterly. It brings order and light out of chaos and obscurity. The content of this section would also have made a valuable volume by itself. It represents a real advance in medical history.

It is impossible even to summarize here the splendid section on Egyptian medicine. Among its more important conclusions is that rational elements in Egyptian medicine must be more stressed than has been done hitherto. On a matter of detail Sigerist accords relatively greater weight—as it seems to us justly—to the rational element in the Ebers papyrus as against the Edwin Smith papyrus. The latter has, he holds, been given a relatively higher grade than it merits because, being surgical, it deals with more obvious lesions than its companion associated with the name of Ebers. All that Sigerist writes on this crux of archaic medicine deserves and will be accorded the greatest respect.

The section on Mesopotamia is much shorter than that on Egypt, but its composition must have been a no less formidable task. So far as publications are concerned the material is less ample though more scattered. The number of unpublished or partly published cuneiform clay tablets in the great national collections is prodigious.

[1] *A History of Medicine*. Volume 1: Primitive and Archaic Medicine. By Henry E. Sigerist, M.D., D.Litt., LL.D., Dr.h.c. (Pp. 564; 48 illustrations. £2 5s.) London: Geoffrey Cumberlege (Oxford University Press). 1951.

From the library at Nineveh of the scholar-emperor Ashurbanipal (668–626 B.C.) there are 22,000 tablets in the British Museum alone. It is to this collection, still imperfectly explored, that we owe most of our knowledge of ancient Mesopotamian medicine. No one can even guess what light may be thrown on the subject from this and other collections when they have been fully read and adequately interpreted by specialist scholars. In any event Sigerist has expounded in a manner that is beyond praise the setting and the social environment against which such discoveries must be viewed.

Matters for criticism are few and none of importance. We doubt if such generalizations as the belief in a soul among all "primitives" can be fully justified. We miss reference to the civilizations of North-west India. Their antiquity rivals that of the other great river-valley cultures, and their sanitary conditions and cultural background are relevant to the discussion. The medicine of the Vedas, especially the Rigveda, also comes within the "archaic" period and within the geographical area with which this volume is, in the main, concerned. Doubtless the ancient Indus civilization and that of the Vedas will be used as an introduction to Indian medicine.

This is a major work that raises the study of medical history to an altogether new level. The reviewer feels that he must end his inadequate notice of this splendid volume with a personal note. Many years ago he formed the hope that the history of medicine would attain, as a subject, the coherence and dignity of an academic discipline. This it has not hitherto reached. In his judgment its chief need has been a large-scale authoritative survey. Dr. Sigerist is the only man living capable of providing it. Many books have been written with the title "A History of Medicine." This is the first to deserve the title, for it is the first to be written in full social perspective. When it is completed, medicine will be in a position to re-enter the circle of the "humanities" of which it was once an honoured member. For medicine is not only an art and a science, it is also one of the great humanities. Its history will find its rightful place in that greatly needed addition to the medical curriculum, a course on the ethics and social implications of medical practice.

## RECENT TECHNICAL DEVELOPMENTS

*Methods in Medical Research.* Volume 3. Editor-in-Chief, Ralph W. Gerard, M.D., Ph.D. (Pp. 312. $7.) Chicago: Year Book Publishers Inc. 1950.

This is the third of a valuable American series of year-books dealing with the details of modern technical methods used in researches in medicine and in a wide range of the related disciplines of biology, chemistry, and physics. The series is planned by a board of American and Canadian leaders in different parts of the general field, and each year's volume has a general editor, in this case Professor Gerard, and an associate editor for each of its three or four main sections. It will be clear that this series has no resemblance to one of those massive, systematic, "technical handbooks" issued in an apparently unending succession of instalments. The governing board lays plans each year for a handy year-book—about 300 pp. in the present instance—of three or four main sections, dealing apparently with quite unrelated subjects, and each consisting of a number of short articles by experts directly concerned with recent technical developments.

The volume under review, that presumably for 1950, consists of sections on genetics of micro-organisms, assay of neurohumors, selected psychomotor measurement methods, and methods for the study of peptide structure. It must be presumed that the board plans a volume to contain what is ready, or what it regards as urgent or topical. This gives assurance that each will be well up to date; but some prospective purchasers may find it inconvenient to acquire the whole series to ensure that they will not miss sections concerning their special interests. It is not every experimental psychologist, one may surmise, who will require details of technique for researches on bacterial genes, chemical transmitters, or peptide chemistry. But the plan—that of a journal rather than a handbook—guarantees freshness and immediacy of interest, and its explicit object is to deal with the practical details of methods, for which ordinary journals can seldom find room.

The quality of the articles in the present volume, so far as one observer can judge, is of the high standard to be expected of the authors and editors. As a personal reaction, I have doubts about "neurohumors" in the sense in which it figures in the title of Professor Gaddum's section. I like it as an act of piety to the memory of my friend of many years, the late Walter Cannon; but I am not sure whether Cannon himself meant the term to be applied to a chemical transmitter as exercising its closely localized physiological function, or in accidental and literally humoral transport to other organs, as he detected it.

H. H. DALE.

## PHYSIOLOGY AND BEHAVIOUR

*Symposia of the Society for Experimental Biology.* No. 4: Physiological Mechanisms in Animal Behaviour. (Pp. 482; illustrated. £1 15s.) London: Cambridge University Press.

This substantial volume is a report of a joint symposium held in Cambridge in 1949 by the Society for Experimental Biology and the Association for the Study of Animal Behaviour. It is unique in that it contains a great deal of information which is not elsewhere readily available in English, or indeed in any other language. The science of comparative ethology, as the study of animal behaviour is now termed, has been making rapid advances in recent years; now it is nearing that stimulating stage when the approaches of the behaviour student and the neurophysiologist are bringing them sufficiently close to make joint discussion both profitable and exciting. Although the present volume is mainly concerned with animal behaviour, it links up in innumerable ways with the study of human behaviour, and it is to be hoped that it will be widely read not only by human neurophysiologists but also by psychologists.

The subject is considered under three main headings: (1) The range and capabilities of sense organs, in which special attention is paid to hearing, vision, and proprioceptors; (2) the problem of peripheral versus central control of behaviour co-ordination; and (3) the whole problem of instinct in the modern sense and its relation to recent experimental and theoretical advances in the study of learning.

It seems safe to say this book will be indispensable to all workers in these and cognate fields and that it will be a long time before it is superseded.

W. H. THORPE.

## PSYCHOLOGICAL TYPES

*Personality and Psychosis.* By Otho W. S. Fitzgerald, M.A., M.D. (Dubl.). (Pp. 134. 12s. 6d.) London: Baillière, Tindall and Cox. 1951.

The grouping of personalities into types has made possible a system of critical comparison between personalities possessing different traits. Thus we have Jung's general attitude types of extraversion and introversion and Kretschmer's cyclothymes and schizothymes. The author's aim in this book is to construct hypothetical personality types, composed of a limited number of traits, so that each personality type is analogous to a psychotic syndrome. In this way the study of the pre-psychotic personality can be made more exact.

The author finds Jung's type theory, which is based on the notion of mental energy, best suited to his purpose. He formulates two basic traits—objectivity and subjectivity of interest, meant to correspond roughly with Jung's extraversion and introversion. Abhorrence of new terminology is the reason for adopting Jung's terms, but the connotation given here to extraversion and introversion bears little resemblance to Jung's use of the words.

The author describes three genetic types of personality found in the pre-psychotic individual: the impetuous extravert, the deliberate extravert, and the introvert personality. These relate respectively to the manic, melancholic, and schizophrenic psychoses. There are also three acquired traits—hysteric, obsessional, and paranoid. The acquired traits may be combined with any of the genetic types. A descriptive nomenclature is achieved in consequence of this blending, and this provides a diagnostic description of psychotic syndromes.

With pre-psychotic patients it is easy, in retrospect, to recognize personality traits. But many so-called normal people, who never become psychotic, have the same traits, although in a mild form. The drawback to the term pre-psychotic is that we can rarely say when the "pre" stage begins, and so its value in preventive therapy is small. The best part of the book is the case histories. They reveal the author as an acute observer with a facility for the right phrase. The index is inaccurate and unworthy of the book.

E. A. BENNET.

## TEXTBOOK OF SURGERY

*Wullstein–Wilms Lehrbuch der Chirurgie.* By Professor E. Gohrbandt, Professor E. v. Redwitz, and Professor F. Sauerbruch. Volumes 1 and 2. Tenth edition. (Pp. 1,600: 121 figures. M. 98.) Jena: Gustav Fischer. 1951.

This is the tenth edition of a work which for over forty years has been the outstanding German textbook of surgery. Many of the leading surgeons of Germany in that period have shared in its production, and among them are the great names of Wilms, Perthes, de Quervain, and Schmieden. The most distinguished of all, Professor Sauerbruch, has recently died, but lived to share in the production of the latest edition of this great work.

Although considerably enlarged and to a great extent rewritten, it remains essentially a textbook for students. The basic principles of surgery are discussed in the thorough manner characteristic of the German mind, and these are illustrated from an immense wealth of clinical material with plates and diagrams of the highest order. The use of antibiotics is very fully described, but more recent advances in surgery are considered very briefly. It is noticeable that scarcely any reference is made to work outside Germany itself. Perhaps the long isolation of Germany made that unavoidable.

The production of these volumes under difficulties which few of us can appreciate is a great achievement, and they supply the German student of the future with a solid foundation upon which to build. Indeed, any young British surgeon who cares to devote to them the careful study which they deserve will be amply rewarded.

HENRY SOUTTAR

## BOOKS RECEIVED

*Review is not precluded by notice here of books recently received*

*Good Health with Diabetes.* By I. Murray, M.D., F.R.F.P.S.G., F.R.C.P.Ed., and M. B. Muir, S.R.N. 2nd ed. (Pp. 44. 2s.) Edinburgh: E. and S. Livingstone. 1951.

*Bacterial and Virus Diseases.* By H. J. Parish, M.D., F.R.C.P.Ed., D.P.H. 2nd ed. (Pp. 204. 10s. 6d.) Edinburgh: E. and S. Livingstone. 1951.

*Medical Botany.* By A. Nelson. Ph.D., D.Sc., F.R.S.Ed. (Pp. 544. 30s.) Edinburgh: E. and S. Livingstone. 1951.

*Emotional Security.* By M. R. Sapirstein, M.D. (Pp. 291. 16s.) London: Rider. 1951.

*The Medicough Papers.* By H. Ross. (Pp. 264. 10s. 6d.) London: Andrew Dakers. 1951.

*Recipes for Light Diets.* By E. M. Shipley, B.Sc., and H. M. Dundas. (Pp. 38. 3s. 6d.) London: J. and A. Churchill. 1951.

*Army Medical Library Classification.* (Pp. 275. $1.25.) Washington, D.C.: Superintendent of Documents, U.S. Government Printing Office. 1951.

*Cardiopatologia.* By Dr. J. A. A. Mateo. (Pp 101. 25 pesetas.) Barcelona: Byp. 1951.

*Fortschritte in der Behandlung Schwerer und Schwerster Hochspannungsunfälle.* By Professor H. Fischer and Dr. R. Fröhlicher. (Pp. 72. M. 10.80.) Stuttgart: Georg Thieme. 1951.

*L'Allongement Vertébral des Rhumatisants.* By Dr. A. de Sambucy and M. de Sambucy. (Pp. 138. 800 francs.) Paris: Librairie le François. 1951.

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As Mr. Berry says in his foreword to *The Law Relating to Mental Treatment and the Health Service* (J. and A. Churchill. 8s. 6d.), the size and importance of the problem of mental disorder are not generally realized. In England and Wales there are about 200,700 mental hospital beds as against some 315,000 general hospital beds for all other types of illness. This little book is designed to provide, for the benefit of general practitioners and all those whose work brings them face to face with the problem of mental illness, a guide through the thicket of legislation which surrounds the subject, and to show what each must, may, and must not do in his dealings with the patient. It would provide an even better guide than it does if it contained an index, for which its full table of contents is no real substitute. Mr. Berry discusses clearly and comprehensively the recent changes in the law which follow upon the National Health Service Act, 1946, and the Criminal Justice Act, 1948, which, as he points out, make a real advance in the way in which mental disorder can be dealt with in the administration of justice, at any rate in courts of summary jurisdiction. Many will feel, however, that in his comments on psychiatric evidence in capital cases Mr. Berry has done less than justice to prison medical officers, though otherwise he has dealt with this very contentious subject with creditable objectivity and restraint.

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## SOCIAL NEEDS AND MODERN WAR

However diverse the meanings of "democracy" in different longitudes, in the West it implies free access to records and the right to expose errors and miscalculations. It facilitates candour in judging the conduct of authorities. An example of that liberty to examine and assess is to be found in Professor R. M. Titmuss's contribution to the "Civil History" of the second world war.[1] The historian who writes before the ink is dry on the current accumulation of wartime reports almost inevitably assumes something of the character of prosecuting counsel. He must use files in which all the complaints pile up and few successes find mention. He cites official statements and can draw a damning picture; a judicial summing-up is for the future. In the meantime blame for mistakes can be freely apportioned among all concerned: the Treasury, whose insensibility to human relations is underlined, whose ineptitude is tellingly if a little unfairly pilloried in quotations, whose prescience is parodied; the local authorities, whose continued entanglement in Poor Law futilities will come as a surprise to those who thought that relic of Tudor times was dead and buried; the Ministry of Health, seeking, with no experience of administering hospitals and no staff with training for the purpose, to accomplish an evolution in the time-space of a revolution; the voluntary hospitals, preoccupied with preservation of their finances to the exclusion of urgently ill men, women, and children. All these, and others, can here read the long list of their blunders: not even the London County Council escapes mild censure.

Despite all the vacillations and want of clear thought that marked advance preparations for war on a civilian population, and that dogged the groping and sometimes half-hearted efforts to make good earlier deficiencies—and here it must be remembered that the participants in this harassing situation were called upon to do the work of sixty years in six, and to do it when experienced staff were being spirited away overnight—the ultimate result was a great advance in the "material" of social services as well as better understanding of their fundamental principles. It was partly enforced by the pressure of the people's own common sense and their determination to get and give fair play. The bombs themselves did much to blast away ignorance about prewar conditions of poverty and undernourishment and to bring to light the hidden needs of the sick. It became clear long ago that the plans for evacuation and for the treatment of casualties were misconceived because of the widely erroneous appreciation by the Service experts of the nature and weight of the expected attack; but that was not the whole story. The psychologists were led astray by the scanty evidence from bombing in 1917–18 and by fallacious reports from Spain. They expected panic, for they underestimated the strength of family cohesion, but they gave no warning of the emotional disturbance that would result from mixing urban and rural populations, from two standards of clothing, cleanliness, and house-training in the same dwelling. We of the medical profession were ill-informed of the standards of different types of hospital and institution, and insufficiently aware of the extent to which health, sickness, recovery, and the return to work were social as well as clinical problems: and if that statement appears an exaggeration it is just because the lesson has been driven home and learnt so thoroughly in a few years.

The pages of Professor Titmuss's book are well documented and illuminated by many vividly phrased comments and instructive footnotes. As there are some twenty-two or more volumes of the History to come, and overlapping is unavoidable, three main themes are selected for record—evacuation, the care of the homeless, and the Emergency Medical Service. The last-named will of course receive detailed treatment in the "Medical History." Evacuation occurred in three phases: at the outbreak of war, again in 1940, and once more in 1944. It was not all "official." More than 1,250,000 voluntary evacuees complicated the issue by moving into the reception areas. Actual compulsion was never exerted, though exhortation was forceful at times. The second effort was largely successful where the first "failed," partly because the bombs were an argument it was difficult to counter, but much more because experience had taught the need for screening both parties—those who arrived and those who gave housing and help. Amid all the official efforts to provide for real needs, which were by no means exclusively related to statutory destitution or social standing, it was welcome and certainly not unexpected to find how great a share of neighbourly care and help was afforded by a host of voluntary agencies, among which the Women's Voluntary Services take so honourable a place. Nobody is likely to forget the outcry over the distresses that characterized the first evacuation. Titmuss cites many examples both of

[1] *Problems of Social Policy*, 1950, H.M.S.O., London. Price 25s.
[2] See annotation in *British Medical Journal*, 1951, **2**, 410.

the stupidity and of the misfortune that intensified dissatisfaction. When large numbers of children travel long distances in non-corridor trains mishaps must be frequent: the unfortunate evacuees will arrive miserable and ashamed, and foster parents will get a bad impression of the arrivals. Nevertheless, the Treasury, with a planned evacuation of four million refugees, thought provision of temporary sanitary conveniences at railway stations "a waste of money." Ill-clad and ill-shod schoolchildren arrived in numbers in rural areas. Authorities were "authorized to make purchases locally of boots, clothing, and knapsacks up to £1 for every 200 children." The lack of blankets was just as distressing. Homes, hostels, nurseries, maternity homes, convalescent homes, schools, and other shelter were an obvious necessity, but requisitioning from all quarters was so ill-coordinated that "the central register virtually broke down."

The Emergency Medical Service, from an indifferent start, became a great success, but at a cost. Besides accomplishing its immediate task of caring for wounded—civil and military—and for some priority classes, it developed the first form of a national hospital system and almost the earliest and certainly the most comprehensive regional services yet attempted. It demonstrated, on a large scale, the social accompaniments of clinical methods for returning men and women fit to their occupations, and it proved the efficiency of special centres in the care of experts. These and many other benefits are now part of the permanent hospital service, but there is no disguising the fact that hospital treatment was denied during the war to many who needed it, not least the aged and infirm. The argument was irrefutable that, whatever war might condone, there ought not to be any discrimination between sections of the community in the availability and the quality of medical services—preventive, remedial, or restorative. Perhaps the effort to put this into practice was too hurried and insufficiently thought out, but the urge was irresistible. For the remarkable wartime health records credit is given not to the medical profession but almost wholly to the Government's social activities—most of all to the measures for controlling food supplies and for the distribution of milk to children and nursing mothers. That full employment on good pay, continuing over three or four years, played a part in eliminating health hazards is admitted. It is at all events noteworthy that for the first eighteen months or two years death rates and notifications of infectious disease tended to fall; and that despite bombing, with all it entailed, from 1941 onwards, when the social measures began to operate, almost everywhere improved figures appear on the records except in the case of tuberculosis. The social historian finds, however, that since no country hitherto has had nation-wide morbidity statistics there is difficulty in making comparisons with previous periods. The General Register Office has begun, in association with W.H.O., to plan the machinery for such records.

Running through this whole story of social policy in wartime is the tale of the dead hand of excessive "localism" and the paralysing influence of narrow boundaries. Even more inimical to the interests of the sick and the "convalescent," and those in need of social assistance, are the "means tests" (of which there were at one time no less than twenty in use) and assessments. Titmuss states that the L.C.C. recovered 10% of its expenditure over a few months on transferred cases, the administrative cost of assessment being 23.9%. Apparently the same disproportion occurred in great numbers of inter-authority claims and reclaims. There are difficulties in the Health Service to-day which can still be attributed to over-meticulousness about petty financial adjustments. Some administrators are tempted to avoid trouble at the "expense" of patients' needs. If preparations have to be made for another war (in this connexion the Ministry of Health has just issued a memorandum to local authorities on their duties in relation to the casualty services and to the public health in time of war[2]), local obsessions about boundaries between authorities must not be allowed to influence the administration. It should also be borne in mind that disruption of the family is often a worse evil than the hazard for its members of death together; that deprivation of the accustomed environment is a potent source of harm for the young which can exert its effects to the third generation; and that the cost of war is not reckoned until the share that falls upon the sick, the elderly, and the infirm is included.

## PREVENTING SHOCK WITH DEXTRAN

The value of blood and plasma in saving life by the prevention of surgical shock is now so familiar as to be commonplace, and the arrangements for supplying these vital fluids in Britain are so excellent that we are inclined to forget that expense or stark non-availability limits their use in much of the rest of the world. Even in Britain, if modern war were to afflict us, a relative shortage would certainly be felt. Viewed against this background, complete investigation and trial of other colloidal materials suitable for intravenous infusion acquire importance, while the possibility that jaundice is not the only untoward long-term result following the use of plasma (or even of blood) should not be overlooked.

In this country, dextran is at present regarded as satisfying adequately the criteria of a plasma substitute. Experience with the British-made material issued through the Transfusion Service has been satisfactory, and has not altered the attitude of cautious optimism expressed[1] when the first clinical trials from this country were reported. In a carefully observed series of patients treated in a burns unit Bull[2] has since been able to show that the proportion of patients surviving when dextran solutions were used closely approximated to the results expected on the basis of a statistical study of patients similarly treated with plasma during preceding years.[3] Experience in Sweden with Swedish-made material has been even more extensive and widely reported (see, for example, [4]), though comparisons with plasma are not readily available there, as it is little used. For the treatment of burns it is generally agreed in this country that plasma or a plasma substitute is indicated, with blood in addition only in cases with very extensive or deep burns. In other traumatic injuries blood loss is usually the main factor liable to cause shock, and ideally blood replacement is required. If blood is not available dextran (or plasma) will maintain blood pressure and circulation,[5] but with very considerable red cell losses the haemo-dilution accompanying this treatment may be serious (in animal experiments even dangerous). For the present, therefore, it would seem wise to limit the amount of dextran infused under such circumstances to, say, two to three bottles (500 ml. each), blood being then obtained for administration to all patients with major haemorrhage. Even for treating burned patients (who require, on average, 1–1½ litres of dextran or plasma for each 10% of the body area burned), the amount of dextran administered should if possible be limited to five or six bottles (proportionately less in children), plasma then being used if necessary, since excessive replacement of plasma proteins with the polysaccharide dextran is probably undesirable.

A most important proviso with regard to any plasma substitute is that it shall contain mainly the correct size of colloidal molecule—in most cases, something of the order of molecular weight of albumin (i.e., 72,000); to ensure consistency of material, this implies manufacture to specification. All of the plasma substitutes at present under consideration (dextran, polyvinyl pyrrolidone, gelatin) contain mixtures of molecules ranging from comparatively small to larger sizes. Small molecules tend to escape rapidly from the circulation and are lost from the body into the urine, so that their therapeutic effect is transient.[7 8] Very large molecules are inefficient in that they have a low osmotic effect for a given weight of material, cause some degree of aggregation of red blood corpuscles,[8-10] and, at least in the case of some chemical substances, may cause damage to blood vessels, etc.[6] Dextran, as provided by the transfusion service in this country, has been carefully tested by quantitative animal excretion tests so that less than 25% of the material escapes into the urine, and by viscosity tests to limit its content of large molecular material.

Much still remains to be learned of the behaviour of colloids like dextran in the body, and it is the duty of experimental pathologists and others to work on these problems. The removal of dextran from the blood stream in the days following its administration and its gradual disappearance from the body are being further studied following the report already mentioned[1]; quantitative excretion[7] and renal clearance studies[8] have been carried out with dextran; red cell aggregation has been studied in detail in Sweden[9] and in this country.[8 10] Dextran labelled with radioactive isotopes should make the precise location of dextran in all studies of this kind technically much simpler. Although dextran is non-antigenic, it can act as a haptene and might theoretically induce reactions in patients sensitized by the micro-organism, *Leuconostoc*, which makes it, or by others antigenically related to it. Although a careful watch has been kept for such untoward effects, none has been reported as yet in this country. Medical opinion here is rightly cautious about all new therapeutic substances, but dextran is beginning to show signs of standing the test of experience.

One practical point requires emphasis. Two or three ml. of blood should be withdrawn and kept from every patient about to receive dextran. This enables blood grouping and cross-matching to be carried out with the usual technical ease if administration of blood is called for within the next few days.

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## THE RISKS OF MATERNAL RUBELLA

Maternal rubella in the early months of pregnancy is apparently thought by some to necessitate termination of the pregnancy. It has been suggested that abortion for this purpose is probably illegal,[1] and, apart from objection on religious grounds, the medical evidence can hardly be taken to justify such a course. It is true that Swan and his colleagues[2] published

figures to show that if a woman has rubella in the first or second month of pregnancy the baby will certainly be abnormal, while if the illness is in the third month one out of every two babies will be abnormal. Even as long ago as 1882 the birth of an abnormal baby was observed after maternal rubella,[3] and confirmation of the association has been received from many countries besides Australia, but Swan's figures referred to a particularly severe epidemic in a particular country, and in other circumstances they may well be inapplicable. Writing in 1949, Swan[4] concluded, on the grounds that three out of four babies will probably be abnormal, that abortion was justified when a mother has rubella in the first four months of a pregnancy. Besides the risk of congenital deformities babies who have been exposed to rubella in their early embryonic period are often difficult to feed.[5] But before deciding that termination of pregnancy is necessary in such cases the doctor must consider the nature of the infants' handicaps. Abel and van Dellen[6] reported that of a series of 84 babies in the U.S.A. whose mothers had rubella in pregnancy, 56 were abnormal. However, only seven of these were mentally defective. Again, the congenital heart lesions seen after maternal rubella are predominantly acyanotic ones, such as patent ductus arteriosus, and cataracts are sometimes unilateral and are to some extent amenable to treatment by needling or lens extraction. In Abel and van Dellen's series the listed deformity in 5 of the 56 affected cases was "malformation of the teeth." Apart from these considerations, other authors have not found the chances as high as did Swan that abnormal children will be born. Patrick,[7] considering children born in Australia in 1941, estimated that 49% were affected when the mother had had rubella in the first trimester. In the U.S.A. Fox and Bortin[8] found that of 11 pregnant women who had rubella in 1942–4, only two gave birth to abnormal children. These two mothers had been affected in the first or second month, but three others who had rubella in the second month and three in the third month had normal babies. Ober and his colleagues,[9] also in the U.S.A., concluded that, of live babies born to mothers having had rubella in the first three months, 50% were abnormal, and in the fourth to ninth months, 14%. Grönvall and Selander,[10] in Sweden, found 26 cases of maternal rubella, mostly during the first four months of pregnancy: only one of these mothers gave birth to a malformed child. In England, Bradford Hill and Galloway[11] found, from the records of approved societies, 10 women who had had rubella and later had babies within 12 months of the illness. One with rubella in the first month of her pregnancy had a baby with congenital heart disease, but three with rubella in the third month all had normal children.

The observations of McAllister Gregg,[5] and the later writings of Swan and others have given great impetus to the subject of embryonal and foetal pathology, but our maps of this new continent are still only sketch maps. In general, it is probably justifiable to say that if a woman has rubella during the first three months of her pregnancy there is a serious chance—perhaps 25%, perhaps over 80%—of her baby having one or more abnormalities and that such abnormalities may be serious, such as microcephaly and mental deficiency, or less important—from a patent ductus arteriosus to malformed teeth. It is good to know that further evidence likely to be statistically reliable is being collected.[12] When it comes to considering the risks to the foetus of maternal illnesses during pregnancy other than rubella, all that can be said is that the incidence of abnormalities is higher after such illnesses,[13] though in any individual cases the danger is not such as to justify great anxiety.

One way of preventing malformations due to maternal rubella would be to ensure that all girls have rubella before they grow up. They could be intentionally exposed by contact when opportunity offered. Anderson[14] has shown that the virus can be transmitted at will by inhalation of atomized throat washings, and that the virus can be preserved active for three months. Although rubella may be followed by neuritis or encephalomyelitis, such complications are "of great rarity,"[15] much rarer than in measles.[16] Rubella may occur without a rash, and it may be difficult to ensure that a susceptible pregnant woman is not unwittingly exposed: nor does every woman realize she is pregnant during the first month. But if a susceptible pregnant woman is exposed to infection she should be protected with gamma-globulin: 2 ml. of serum from a patient convalescent from rubella is a suitable dose. If rubella does occur, then it is important that the anxieties, if present, of the parents should be relieved as much as possible by letting them know that they are quite likely to have a normal baby, and that, if the baby is affected, it will not necessarily be seriously.


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## PSYCHOTHERAPY IN PRISON

In the report[1] of the Commissioners of Prisons for the year 1949 an interesting account is given of pilot studies in the application of psychological methods of treatment. The original survey, which provided the pattern for the present work, was carried out between the years 1934 and 1939 by the late Dr. W. H. de B. Hubert, under the direction of Sir Norwood East, and provided ample grounds for believing that psychotherapeutic methods would be valuable in the treatment of delinquency, even in the prison environment. In the report by East and Hubert[2] there was a recommendation that a special institution should be provided for the care, study, and treatment of selected groups of prisoners of carefully defined classes. Recent progress in more than one field of psychiatry confirms the importance of that recommendation.

As appears from the recent report, psychotherapeutic work, which ceased at the outbreak of war, was begun again in 1943 and has been in the hands of two psychiatrists—Dr. J. C. Mackwood and Dr. J. H. Gould. They have been severally occupied with cases of rather different kinds and have employed different methods.

During the five years covered by the report Dr. Mackwood saw 244 cases. In some of these there was mental subnormality and in others a degree of psychopathy which would interfere with treatment; in all 90 prisoners were accepted for treatment, and 67 were substantially or greatly improved. Apart from constitutional abnormality there may be other causes which impede treatment. The inhibited, timid, and cowed individual who has been emotionally isolated all his life suffers in prison from the attitude of more aggressive prisoners. If his own aggressiveness comes to the surface he may be involved in fights and punished equally with others, and thereby suffer a setback. The interesting case is quoted of a lad who was in prison for larceny, having stolen women's clothes for fetishistic purposes. As a result of treatment he became bolder and more self-reliant, but got into prison fights, and after discharge broke into an empty flat and spent a week-end living well in a fully heterosexual life with his girl friend. Psychological improvement brought with it an enhanced risk to the community. The problem posed by such cases, which cannot be infrequent, is by no means easy of solution.

Group treatment was begun in 1946, and it was found possible to treat in this way men who would have been unsuitable patients for individual psychotherapy. The group provided a substitute for the gang that is likely to form when a heterogeneous collection of prisoners is massed together, and group morale is a basis for the development of a social conscience.

Psychotherapy in the prison environment is in some respects easier and in some more difficult than outside. A man with a long sentence, for instance, may be in the right mood to co-operate immediately after sentence, but if treated then may later become stale. It has occasionally been possible to secure earlier discharge for such patients after successful treatment. It is clear that in working with prisoners the psychiatrist tends to form views about the value for the growth of personality of other circumstances of their lives, and is inclined to propose administrative changes, such as transfer to a prison of a special type. In so far as it is realistic, and so proves itself in practice, the medical approach to penology will be found to exercise gradual but far-reaching effects.

Whereas Dr. Mackwood principally employed psychotherapeutic methods based on a psycho-analytic type of psychodynamic theory, Dr. Gould describes the application over two years of methods of other kinds, including electroplexy, hypnosis, narco-analysis, and ether abreaction. Of the 78 patients seen by Dr. Gould no fewer than 39 were found to be suffering from a psychosis, and it was no doubt for this group that electroplexy was principally used. Ether abreaction, first used by Palmer and later further developed by Sargant and Shorvon for the treatment of neurotic casualties in war, was of greatest value in those patients whose illness had been precipitated by a single severe traumatic experience. The prisoners who were chosen for this treatment were those in whom there had been a damming up of tensions centring on some single focus. One such case is described; this prisoner's neurosis actually began during active hostilities and resulted in fugue states and a hysterical paralysis, as well as in delinquency in the form of forgery of a bank-book. The abreactive treatment resulted in a release of energy which could be satisfied only by the hardest forms of manual work. Once again it is to be noted with interest that psychiatric findings resulted in an administrative change, and the man was transferred to a prison where his special needs could be met.

The reader of this report becomes aware that he is witnessing only the beginning of what are likely to prove fundamentally new lines of growth in penology. Once sentence has been passed the individual characteristics of the prisoner are claiming an increasing share of attention, while the nature of his crime tends to recede into the background. The psychiatric methods of treatment which have been used so far, and which are described in this report, are by no means the only ones that may in future be considered. Recent research —for instance, the electro-encephalographic studies of prisoners, by Stafford-Clark and Taylor[3]—indicates that some crimes of violence, especially those in which the motive is obscure, are related to physiological dysfunctions of the brain, and may be preventable by medical measures. It is to be hoped that it will eventually be possible to establish a special institute of treatment and research within the frame of the prison administration, and that its functions will be much wider than merely a concern with the psychodynamic aspects of crime.

[1] Report of the Commissioners of Prisons for the Year 1949, H.M.S.O., London.

[2] *The Psychological Treatment of Crime*, 1939, H.M.S.O., London.

[3] *J. Neurol. Neurosurg. Psychiat.*, 1949, **12**, 325. See also annotation in the *British Medical Journal*, 1950, **1**, 361.

## HEALTH IN 1949

Babies born in England and Wales in 1949 had a better chance of surviving to their first birthday than ever before. The infant mortality rate was 32.37 per 1,000 related live births—a rate improved upon in 1950, when it was 29.8 (provisional figure). For younger people particularly 1949 was a healthy year. According to the Chief Medical Officer of the Ministry of Health,[1] though the overall mortality was higher than in 1948, at ages under 45 death rates were in general lower. He concludes that the increase in the death rate for all ages combined "signified no more than the normal effects of climatic and epidemic variations on older people." Increases in the death rate were mainly due to heart and vascular diseases, influenza, and respiratory diseases. These, together with old age, accounted for 61.2% of all deaths in the year—nearly 4% more than in 1948. Mortality from cancer among females declined. Mortality from cancer among males increased, but this increase was due to deaths from cancer of the lungs and bronchi; mortality from cancer at other sites in males declined. The epidemic of poliomyelitis, which caused 5,967 cases and 657 deaths, was second only to the 1947 epidemic in severity, though the number of deaths did not equal the total from measles and whooping-cough combined (834).

From January 1, 1949, medical officers of health were for the first time required to include notifications of food-poisoning cases in their weekly returns to the General Register Office, and this was a timely measure, for it was known that the incidence had been increasing during the previous ten years. During the year 6,111 cases were notified, but additional evidence showed that there were at least 11,000 cases, despite the fact that in many outbreaks the number of persons attacked was not known. The seasonal incidence is notable. Of the known cases 229 occurred in the first quarter, 398 in the second, 1,006 in the third, and 649 in the fourth. Much the commonest infecting organism was *Salmonella typhimurium*; other salmonellae accounted for 326 cases and staphylococci for 97. The danger of eating in restaurants proves to be much less than is commonly thought. Out of 218 outbreaks in which the place of infection was known, only 35 were caused by eating in commercial catering establishments; and, though about a quarter of a million main meals were served daily in over 1,000 catering establishments in the City of London, no outbreak of food-poisoning was notified.

The Chief Medical Officer attributes the increased incidence of food-poisoning mainly to three causes. The first, due to economy in using rationed meat supplies, is the retention overnight and reheating of meat dishes cooked the previous day. The second is the great increase in communal feeding in schools, mines, and factory canteens. Here again the food is cooked in large containers the day before it is eaten, and while cooling remains for a long time at a temperature favourable to the rapid multiplication of organisms; the temperature to which the food is reheated is too low to kill them. The third cause is neglect of personal hygiene, often due to lack of facilities, rationing of supplies, and shortage of staff. In this connexion some useful practical points for kitchen and dining-room workers are clearly described in a recent Ministry of Health circular to hospitals (H.M.C. (51) 79).

Immunization has now made diphtheria a rather uncommon disease, but once contracted it is no less dangerous than formerly. Though there were only 1,890 cases in 1949 as compared with about 65,000 in 1938, the number of deaths per 100 notifications was the same —4.4. This is the more surprising in view of the benefit that might have been expected from antibiotics, and also because investigations have shown that whereas *mitis* strains increased in frequency between 1945 and 1948 *gravis* and *intermedius* strains decreased.

As we have come to expect that it should, the nation's health continued in general to show a steady improvement in 1949—in spite of some astonishing climatic vagaries. April 16 was hotter than any recorded April day; there have been only two drier summers at Kew since records began in 1871; and October was the wettest since 1903. But "the year, alike at its beginning and end, was remarkably free from fog."

[1] *Report of the Ministry of Health for the Year ended March 31, 1950.* Part 2 (Annual Report of the Chief Medical Officer for the Year 1949). H.M.S.O. 6s.

## HELPING THE HANDICAPPED

In the history of social reform it is common to find the State or local authorities taking over and developing welfare services which owed their origin to voluntary effort. A recent instruction[1] from the Ministry of Health to local authorities illustrates this process. Under the National Assistance Act, 1948, local authorities are empowered to assist "handicapped" persons in various ways, but so far the only statutory duty laid on them (thirty years ago) is to provide a welfare service for the blind.[2] Now they are to be permitted to organize schemes to help the deaf, the hard of hearing, and those handicapped by a wide variety of disabilities. The deaf are those who are born with very defective hearing (often called the deaf and dumb), and there are thought to be about 25,000 of them. There are in addition some 250,000 persons so hard of hearing as to need some form of hearing-aid. The type of help which the Ministry will expect local authorities to provide for handicapped persons in general includes assistance to overcome the effects of disabilities and to obtain any preventive or remedial treatment which may be necessary, encouragement to take part in activities of social centres and clubs, and the giving of advice on personal problems. "The deaf," as the Ministry's circular states, "are often unaware of services and facilities available to them or of their rights as citizens."

In planning their schemes local authorities are advised to make the greatest possible use of voluntary help, for of course there are many voluntary bodies with special experience of welfare work among the deaf, the crippled, the paralysed, epileptics, and so on. However good a welfare scheme may be on paper, it will be useless if there is an inadequate information service to make known what can be done to help those who are in need.

[1] Ministry of Health Circular 32/51.
[2] Ministry of Health Circular 87/48 (para. 56).

There are already 900,000 handicapped persons on the register maintained by the Ministry of Labour, but it may well be that the help which can be given under the Disabled Persons (Employment) Acts is still not widely enough known. Elsewhere in this issue Dr. J. A. L. Vaughan Jones describes the admirable training schemes which have been devised to assist crippled or disabled persons to get back into productive work. A most useful conference on "The British Rehabilitation Service," organized by the British Council for Rehabilitation, has been held in London this week, and distinguished speakers—including surgeons, physicians, neurologists, and administrators—have shown that there is no work more rewarding than helping people to overcome physical or mental disability.

## ST. ANTHONY'S FIRE

The outbreak of epidemic madness in the small Provençal village of Pont Saint Esprit is now attributed to ergot poisoning. The chaos and despair in this village of 4,000 people when some 200 of them were seized with a fearful and dangerous disorder, with delirium and hallucinations, have been told in the daily press: according to the reports old and young ran frantic in the streets, and many others lay writhing and screaming on their beds. These descriptions bear a remarkable similarity to those of the mediaeval chroniclers of the mysterious epidemics of St. Anthony's fire that recurred amongst the peasantry of France and Germany. The association with fire has again been noted. Many of the victims suffered from the delusion that they were being consumed by flames.

Since the seventeenth century it has been known that St. Anthony's fire is the result of eating bread made from diseased or "smutty" rye. Ergot is a fungus growing on the ear of rye and much less frequently on other cereals. Infection of rye is commoner following a wet sowing and in a wet summer. The infected ears of rye show long brown or purple spurs among the grains. During thrashing the ergot is removed with the grain, but can be separated owing to its larger size by sieving. In heavy infection as much as a quarter of the weight of the grain may be due to ergot, and as little as two grammes of ergot may cause severe poisoning in man. The recognition of infected rye by the farmer and the miller should be simple, and yet in the present case modern methods of supervision and distribution of flour have not prevented a serious outbreak of ergotism.

The symptoms in the present cases have been chiefly convulsive, but the reports of burning sensations in the limbs suggest that gangrene may also occur. In the Middle Ages the gangrenous form of ergotism was more usual in France, but in each outbreak the severity of the different symptoms varies, and this has led to the description of regional types of the disorder. Any such differences can probably be ascribed to local variations in soil and climate and in strains of rye and infecting fungus that lead to differences in the relative proportions of the toxic components of the ergot. At least five alkaloids, including ergotoxine and ergotamine, amines such as tyramine and histamine, and other active materials including acetylcholine, betaine, and a sapotoxin contribute to the toxic effect of ergot and account for the complexity of the clinical picture.

There have been other recent outbreaks of ergotism. In Russia in the years 1926–7 more than 10,000 people were affected in an epidemic. An outbreak on a much smaller scale occurred in Manchester[1] in 1928. About 200 cases of poisoning were reported amongst Jewish refugees from Central Europe. They had eaten bread made from ergot-infected rye that had been harvested in South Yorkshire. Apart from this outbreak Great Britain has been singularly free from ergotism.[2] The one notable exception was a small outbreak in Wattisham in Suffolk in 1762. This immunity is the result of preferring wheat to rye as a source of flour. Where flour from rye is used on any large scale ergotism will always be a danger, and the disaster at Pont Saint Esprit is a further warning of this risk.

1 Robertson, J., and Ashby, H. T., *British Medical Journal*, 1928, 1, 302.
2 Creighton, C., *A History of Epidemics in Britain*, p. 52. Cambridge, 1891.

## SOUTH BANK MANNERS

The South Bank Exhibition has succeeded in being both instructive and gay, and it is thus all the more disappointing that no effective steps appear to have been taken to meet the justifiable complaints about the food and service at some of the restaurants. Caterers, we know, have great difficulties these days, but, quite apart from the quality of food provided, it is deplorable that many thousands of foreign visitors should have been permitted to see the squalor in which we, as natives, seem happy to eat. Last week at one of the largest cafeteria restaurants the customers had to pick up a tray wherever they could find one. And unless they had a newspaper handy or were prepared to sacrifice a handkerchief they had no choice but to float their plates of food on the slops of previous users of this disgusting piece of equipment. After providing themselves with undried cutlery and sitting down at tables which were only slightly less dirty and strewn with litter than the floor, they were then able to devote themselves to obtaining the maximum enjoyment from their food. Fortunately there are other restaurants at the South Bank where conditions are not quite so bad, but examples of unhygienic sloppiness can be found nearly everywhere. The trays on which the food is taken from the counter are often wet, greasy, rusty, or chipped, and there is usually dirty litter about the floor. Picking up food in the fingers is all too common amongst the staff, about whose other practices a contemporary has recently written: "And why, when everything is new, as at the South Bank and Battersea, should one still see dirty hands and fingernails, greasy aprons, mucky counters, cutlery dropped on the floor and placed straight on plates or food?"[1] The rags which many of the staff carry about in their hands look as if they had been washed out in the river. Surely the least which managements can do is to provide their staffs with clean overalls and dish-cloths. All in all, the South Bank provides an excellent demonstration of some of the common faults in catering hygiene.

1 *New Statesman and Nation*, August 18, p. 172.

## *REFRESHER COURSE FOR GENERAL PRACTITIONERS*

# INDICATIONS FOR AND LIMITATIONS OF PSYCHO-ANALYTIC TREATMENT

BY

**W. CLIFFORD M. SCOTT, M.D., B.Sc., D.P.M.**

*Senior Psychotherapist, Bethlem Royal and Maudsley Hospitals; Director, London Clinic of Psycho-Analysis*

Four questions are usually asked doctors about psycho-analysis by their patients: What is psycho-analysis? Who are psycho-analysts? What is psycho-analysis good for? and How good is psycho-analysis?

### What is Psycho-analysis?

Psycho-analysis is the method of psychiatric treatment or psychotherapy discovered and developed by Sigmund Freud (born Moravia 1856, died London 1939), and developed by his students during the past half-century. The method when used with adults consists of interviews of approximately 50 minutes each, usually five times weekly over many months or a few years. The regularity of treatment is broken by holidays at Christmas, Easter, and midsummer. The number of interviews per annum consequently is between 200 and 240. The patient is asked to lie down on a comfortable couch during the interviews and to talk about everything he is conscious of—to say whatever comes into his mind without attempting in any way to keep anything back. This is what is usually called "free association." The psycho-analyst usually sits just out of the patient's line of vision, but in a position where he can watch the patient's behaviour and hear easily all that he says. As the story of what is on the patient's mind unfolds, comments are made by the psycho-analyst in an attempt to help the patient understand what is happening. These comments are technically called "interpretations."

A situation develops between the patient and the psycho-analyst in which gradually more of the patient's past history, present problems, and plans and hopes for the future are revealed. Gradually the patient is helped to become more and more aware of his capacities to feel and to act. He is helped to understand how his unhealthy or neurotic feelings and actions have their roots in the past, and how they can be overcome by an increased understanding of his development and by increased control of his feelings and behaviour, which is possible for an adult, but was not possible for him as a child. In other words, psycho-analysts have found by experience that sooner or later a picture of the forgotten beginnings of the patient's troubles and a picture of the present-day implications of these forgotten beginnings come to light and in coming to light can be worked with anew. Healthy habits of feeling and activity can be practised and a healthy and more realistic outlook developed.

Much that was "unconscious"—that is, much that had been forgotten or had never been able to become conscious—enters into every psycho-analysis. As it becomes clear which emotional disturbances have been most important in the person's life, it is always found that these self-same emotional difficulties are felt by the patient in and connected with his psycho-analytic treatment. These same emotional problems are also seen in the implications of psycho-analytic treatment in his daily life.

Only when a psycho-analytic treatment is satisfactorily concluded can the patient look back upon the psycho-analytic treatment in an objective, calm manner, and only then can he see the psycho-analyst as a new type of professional individual practising an art or science. The picture the patient has of a psycho-analyst and of psycho-analysis at the end of a period of successful treatment is extremely different from any picture he had obtained by reading or by seeing certain cinema productions or plays. A comparison can be made only with surgery. Only surgeons know what a surgeon's life is—only a psycho-analyst knows what a psycho-analyst's life is. A psycho-analyst's recovered patients come nearest to knowing what a psycho-analyst's life is like.

### Who are Psycho-analysts?

The picture of what patients think of psycho-analysts leads naturally to a consideration of who psycho-analysts are. The early psycho-analysts were the students of Freud, but during the past decades institutes of psycho-analysis to provide training have developed in various countries. The British Medical Association in July, 1929, published the Report of its Psycho-Analysis Committee, which concluded that psycho-analysis, in the strict sense, referred to the technique devised by Freud, who first used the term, and to the theory which had been built up on his work. The committee considered that it was not then in a position to express any agreed opinion either in favour of psycho-analysis or in opposition to it. The claims of its advocates and the criticisms of those who oppose it must, as in other disputed issues, be tested by time, experience, and discussion.

What has been said so far refers to the treatment of adults. During the past few decades psycho-analytic treatment has been used with children. It has been discovered that, by interviewing a child (usually for interviews lasting 40 minutes) regularly in a room fitted out more or less like a nursery, treatment can be started by telling the child that it can say or do whatever it likes so long as it does not hurt itself or the psycho-analyst. The sequence of the child's play and/or talk allows a situation to develop between the child and the psycho-analyst which can be used as profitably as is the situation between the adult and his psycho-analyst where only talk is used.

The institutes which teach psycho-analysis have gradually developed a scheme of education which for the past two decades has been fairly stabilized. Training consists of three parts: (1) a period of personal psycho-analysis; (2) a period of didactic work consisting of lectures and

practical and theoretical seminars; and (3) the psycho-analytic treatment of at least two adult patients under weekly supervision. In Great Britain there is one such institute where at the present time some 60 students are in part-time training, the duration of the course being about four years. Training for the psycho-analysis of children is in addition to and follows that for work with adults.

Only in the United States of America have any of the psycho-analytic institutes become an integrated part of medical postgraduate psychiatric education. In some schools the higher degrees may accredit the psychiatrist as having reached a certain postgraduate standard and as being competent to practise psycho-analysis. In this country the only public accrediting of the satisfactory completion of a course of training at the Institute of Psycho-Analysis is election as an Associate to the British Psycho-Analytic Society. In this country there are about 50 medically qualified psycho-analysts and 30 non-medical psycho-analysts in practice. Their work centres in London, Edinburgh, Manchester, Birmingham, Oxford, and Reading. The society regrets very much that psycho-analysts are scattered so thinly over the country. Psycho-analysts without a medical qualification are those who enter the field from education, psychology, sociology, etc. The board of selection of students, as well as deciding on the student's personal aptitude, requires a university educational standard and advises all students to obtain a medical degree and general psychiatric experience.

The student of psycho-analysis after finishing his training may, of course, do whatever type of work he wishes, except in one instance—a non-medically qualified graduate promises the society not to engage in independent psycho-analytic practice, but only to treat patients who have been referred by a medical practitioner. In recent years an increasing proportion of graduates do not enter whole-time psycho-analytic practice, but combine psycho-analytic practice with child guidance work, work in mental hospitals, work in out-patient psychiatric clinics, work with delinquents, work as teachers in psychiatry, psychology, or social service, etc.

The ambition of all psycho-analysts is, of course, to make treatment more effective and speedier. Experimental variations in treatment are being tried in various places, the chief experiment which is being tried in this country being group psychotherapy—a number of patients (from four to eight) are interviewed together. Although other types of group psychotherapy have a long history, that based on psycho-analytic psychopathology is of such recent origin that there is no agreed opinion amongst psycho-analysts on its use and value. Other experiments have been made in America. The older experiment is based on the hypothesis that psycho-analytic practice and theory are now so definitely established that, after the initial interview with certain patients, one can be reasonably certain what their basic problem is, and instead of embarking on a classical psycho-analysis one can afford to take the bull by the horns, as it were, and put the problem plainly before the patient and at the same time take a role oneself in one's contact with the patient which is quite different from the role previously taken by the people who have caused him difficulty. It is asserted that the adoption of such an attitude towards the patient may result in both good and speedy improvement.

Most psycho-analysts do not consider this type of treatment an advance in psycho-analytic technique, but rather as the application of psycho-analytic principles to that type of psychiatric treatment which is chiefly based on suggestion and re-education. Psycho-analysts, of course, believe that the usual methods of psychiatric treatment can be improved on and speeded up by a knowledge of psycho-analytic psychopathology, which can be put to good use both in the initial interviews with the patient at a time when a decision is being made on what type of treatment should be used and also during the later course of whatever type of treatment is undertaken.

The latest American experimental treatment based on psycho-analysis may turn out to be very significant. It is being applied to the treatment of seriously ill schizophrenic patients, including those whose acute illness is recent and those who have been ill for many years. This experimental treatment departs from classical psycho-analysis in two ways. The initial interview is not short; it is as long as is necessary to obtain contact with the patient and may last practically all day or until the patient falls asleep. Many of the early interviews may be very lengthy. It differs in a second way in the sense that patients may say so little or show such slight activity that there is practically nothing to go on; consequently sometimes stimulation is necessary. The stimulation used is based upon a study of the patient's life and illness. An attempt is made to glean from his history what his most significant problem may be.

It has been found that, if one makes a mistake, the mistake does not seem to matter. What does matter is that one keeps on until one obtains a significant reaction from the patient. Reactions obtained from patients which allow treatment to begin have been found to have been concerned with problems which were significant; in other words, the patients are so used to dealing with people who have been mistaken about their problems that nothing much happens even if another person is mistaken. On the other hand, patients respond very actively to someone who seems to be able to understand even something about their problem. The future of such treatment of severe psychoses will have to await the result of experiments under way during the past six or seven years.

The rate of increase in the number of students training in psycho-analysis has been greatest in the United States of America, but there are still fewer than 1,000 trained psycho-analysts in the whole world. Thus a very long-term view has to be taken, with regard both to the training of psycho-analysts and to psycho-analytic treatment of patients, if a correct perspective is to be maintained. No comparison with any other branch of medicine gives such a good picture as does comparison with general education. A few centuries ago it was believed that universal primary education was an impossible ideal because, first, children were not on the whole educable; secondly, even if children were educable, it would not be a good thing to have a whole population well-educated; and, thirdly, even if children were educable and even if it were considered a good thing to have an educated populace, no country could afford universal education. Now we believe that children are educable (and we take special pains to do everything possible to help those we consider ineducable to make the best of their limited capacities); we believe that it is good for the country for children to be educated; and we

believe that for the sake of the children we must afford their education even to the extent of subsidizing the training of their teachers.

### What is Psycho-analysis Good For?

At present we do not know how many mentally ill people could benefit by psycho-analytic treatment, but psycho-analysts believe that many more could benefit than have the opportunity. Many doubt that psycho-analytic treatment is a good thing at all, but there is increasing evidence to the contrary. Most people feel that psycho-analysis is too costly to have any wide application, but it will be for future generations to decide this point. While we are living in a culture which spends such a large proportion of its productivity in armaments, I do not think it is easy to predict what the future will have to say about the cost of psycho-analysis.

When psycho-analysts think of what psycho-analysis is good for they think much more about altering the patient's basic difficulty in order to allow social, intellectual, and emotional development to take place normally, or to catch up if there has been retardation, rather than just to rid the patient of symptoms. This is especially so with children, in whom it is as yet very difficult on clinical examination to assess whether the presenting neurotic symptoms will be transitory or permanent. It is possible to try to judge during the initial interview or preferably during a trial period of psycho-analysis of a few weeks (10 to 30 interviews) how much intellectual development, emotional development, and social relationships are being interfered with by the symptoms. The need for treatment is more often based on disturbance of development than the seeming severity of the presenting symptoms. The indications for psycho-analytic treatment can be discussed most easily under the heads of hysterical, obsessional, manic-depressive, and schizophrenic disorders.

#### Hysterical Disorder

The first patients treated by psycho-analysis were hysterical—namely, patients with anxieties, fears, hypochondriacal worries about their body, on the one hand, and patients who showed "conversion" symptoms, whose emotional problems were not in the foreground, on the other hand. The "conversion" hysterics—that is, the patients with paralyses, anaesthesias, amnesias, sleep-walking, etc.—were often considered to be showing an abnormally slight emotional reaction to their disability—the so-called *belle indifférence*. The simplest types of sexual complaints belong among the hysterics—namely, some frigidities, some types of impotence, some types of homosexuality in both men and women, some types of sexual perversions, the people who wish to be too submissive or passive or too active and tend to want pain to be connected with sexuality or who tend to have some type of fetish, some special situation or object being necessary before sexuality can be enjoyed. Hysterical symptoms may gradually become incapacitating or they may develop very suddenly and rapidly. Although initially such patients may resist any type of psychiatric treatment, it is with such patients, even though the symptoms may at times be very florid, that psycho-analysis has obtained its best results: best both in terms of speed of recovery and in terms of the change in the persons' whole outlook towards their past, present, and future.

#### Obsessional Disorders

The next most severe group of neuroses are the obsessional disorders, or obsessive compulsive ruminative tension states, in which patients are tense rather than anxious, finding it often difficult to describe their emotional troubles, being worried by their indecisiveness, never being sure that they have done the right thing. Such indecision leads to the typical obsessional behaviour, which may be slight or may be very severe. The patient may have only slight worries about whether or not he has put the right letter in the right envelope, or he must go more than once to be sure that he locked the door, turned off the gas tap, etc. At the other extreme the patient may have a time-consuming ritual which is very annoying to himself—washing incessantly or taking too long preparing to go to bed, etc.

Many such symptoms are not seen in the sphere of action but in the sphere of thinking, such as the patient who cannot decide just what to do or to say or the patient who finds himself ruminating about political or religious or social problems and can never decide just what he should believe, as there is always so much to be said for the other side. Such disorders are, on the whole, more serious than hysterical disorders, and from the description given it is easy to see how much their symptoms are related to what in a lesser degree would be called normal personality traits which might even be an asset in certain occupations. Of course, this is why certain people with what one would call an obsessional personality or character rather than an obsessional illness do such good work and are themselves so satisfied in certain types of responsible routine administrative work. Nowadays, of course, no one can say that we do not need a great many good administrators.

Such obsessional patients are often helped by psycho-analytic treatment, but it is more difficult to measure the degree of help obtained objectively as in the case of hysterical patients. The patient and his family may notice the change, but nevertheless many of the problems which were at one time symptoms may persist, but not in the same form. After improvement the problems are seen in the patient's attitude towards work, play, etc. Whereas before treatment the patient may have been handicapped by his rigidity and fixity and by his desire to follow a strict routine, though during treatment he may have become much less rigid, he may still be known as the type of person he was before, but now as a person with his own special type of personality and not an ill person.

With both the hysterical and obsessional troubles one comes up against the problem that is difficult and serious for the psycho-analyst and difficult for the relatives to understand. The symptoms which present themselves to the patient and are obvious to others are often found to be not so much an indication of the patient's fundamental trouble as an indication of his attempt to cure the trouble. In other words, when a patient begins to realize what his fundamental trouble is and seeks new ways of coping with it, it is quite possible that he finds, when he tries to give up his hysterical or obsessional way of dealing with his trouble, that he is for the time being worse. He cannot easily use his old defences against his emotional trouble, and he has not yet discovered a new, stable, healthier way of dealing with it. This accounts for the fact that a certain number of people under psycho-analytic treatment temporarily worsen.

It is, of course, the responsibility of the psychiatrist and the psycho-analyst to anticipate whether or not significant worsening is a serious danger in any given case. For instance, it is known that many people, if one follows their life histories, oscillate between periods of mild manic-depressive disorder on the one hand and moderately severe obsessional trouble on the other. In other words, a person may be perplexed and rigid and obsessional at one time and at other times he may become depressed, sleepless, and self-reproachful. With such a problem one might say that as the depression lessened he became more obsessional, but it is more correct to put it another way and to say that as his depression lessened he became able to use certain defences against its seriousness, these defences being obsessional.

#### Manic-depressive Disorders

This brings us to the problem of the possibility of psycho-analytic treatment of manic-depressive disorders. These disorders include both the typical depressions with self-reproach and the excited elations with feelings of supranormal fitness, energy, confidence, etc., each accompanied by biological concomitants such as loss of appetite and weight, loss of sexual interest and desire, loss of ability to sleep all night, constipation, etc. Such states vary greatly in intensity. The more severe types present perhaps the second biggest problem mental hospitals have to cope with. The minor states are rarely diagnosed as such.

During the past decade the treatment of such patients by one or other of the physical methods—the chief now being electrical shock—has been to the fore, but at the same time psycho-analytic experimentation has progressed. For several decades some psycho-analysts have been interested in treating the more serious types of mental disorders—the psychoses—and one can at least say that knowledge about the history of the onset of the capacity to be depressed and to grieve is gradually being understood to a greater degree. This knowledge has been put to use in the treatment of depressions, but one can only say that all psycho-analytic treatment of manic-depressive disorders is experimental and difficult. Such treatment is attempted by only a relatively small proportion of the total number of practising psycho-analysts. Some good results have been published.

#### Schizophrenic Disorders

The large group of schizophrenic illnesses in which the disorder progresses by the development of increasing disorganization in the patients' habits and social relations, and progresses step by step to a more and more fantastic outlook on their own and others' lives and the world in which they are living, has been barely touched by psycho-analysts. Those psycho-analysts who have treated most schizophrenic patients have had greatest success by helping patients to increase their ways of repression or ways of hiding their unsolved problems. Only recently have a few psycho-analysts attempted to treat some schizophrenics, first in hospital and then as out-patients, by the classical method. It seems that the more we learn about the basic emotional problems of schizophrenics the more apt we are to be able to help them by classical psycho-analytic methods. The fact that occasionally a patient who has been severely schizophrenic for years seemingly recovers "spontaneously" has always stimulated psycho-analysts to seek what factors are at work in such "spontaneous" recoveries and to bring such factors to work in the psycho-analytic treatment situation.

Those aspects of neuroses or psychoses of children, those aspects of sexual disorders, such as homosexuality, which may not be obviously connected with neurotic symptoms, and those aspects of childhood or adult delinquencies which make psycho-analytic treatment feasible must be left out in an article of this length.

### How Good is Psycho-analytic Treatment?

This question cannot be answered yet to anyone's satisfaction. Everyone would like to see figures and statistics, and would like to see comparisons between psycho-analytic methods and other methods with similar patients. The trouble in assessing results of psycho-analytic treatment is, as I see it, the same trouble which surgery had in its early years. Patients were so dissimilar. No one surgeon had enough patients of a similar type to allow him to make the comparisons he wanted to with other surgeons' work. Specific indications for specific types of surgery have been difficult to arrive at. The various statistics published from the Clinic of Psycho-analysis show results which are just about the same as the results of treatment by other methods of psychotherapy, except that they usually show much better results for hysterical disorders, both anxiety and conversion types. This is not to be taken that all types of psychotherapy are equally good. It only goes to show the difficulties of assessing results—statistical results are still too crude. Again the comparison with surgery has to be made. Psycho-analysis as a technique has been discovered, and its discovery in the long run may be comparable to the discovery of aseptic surgery. It will take generations before statistical methods can be used satisfactorily. For perhaps decades ahead interest will have to remain in the psychopathology and the treatment of the individual patient, and judgments of value will have to be the professional judgments of psycho-analysts, who know both success and failure.

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*Not Least in the Crusade* is an interesting little book by Peter Lovegrove which gives a bird's-eye view of the history of the R.A.M.C. and its predecessors in the space of less than 90 pages. It is amusing to learn that there were over 20 surgeons and a physician present in the English army which won the battle of Agincourt in 1415, and that according to the then prevailing military code they ranked after shoemakers and tailors, but before washerwomen. In the time of Queen Elizabeth army surgeons were usually equivalent to drummers and received the same pay, while if we go back to Edward II, 200 years earlier, we find them receiving fourpence a day (for which they also shaved the men), plus another twopence from each soldier every pay-day. Evidently pay and status have been grumbles of the army medical officer for a very long time. It was Charles II's standing army which first offered doctors a permanent career in the army—though not a very good one—through the purchase of a commission. It is interesting to note that women appeared on the nursing staff of some military hospitals in the second half of the eighteenth century. They were used in the war which attempted to suppress the revolt of the American Colonies in 1757, and there was a regular establishment for them in the expeditionary force which went to the help of Portugal against Spain in 1762—a campaign in which John Hunter served as an army surgeon. The book is illustrated with one colour plate and a number of photographs, and can be obtained from the Editor, Army Medical Services Magazine, Queen Elizabeth Barracks, Crookham, Hants (paper, 1s. 6d., cloth, 5s., plus 6d. postage).

# "BACK TO WORK"

## THE INDUSTRIAL REHABILITATION UNITS OF THE MINISTRY OF LABOUR AND NATIONAL SERVICE

BY

**J. A. L. VAUGHAN JONES, M.B., Ch.B.**

*Regional Medical Adviser, Ministry of Labour and National Service, East and West Ridings*

"Rehabilitation" is a word often used in various contexts. In the realm of medicine it has had a somewhat chequered career, and even now is capable of misconception. It has been divided into such terms as medical or hospital rehabilitation, industrial rehabilitation, resettlement, and that unfortunate term "reablement." However convenient this may be from departmental, sectional, or other angles, it is essential to recognize that "rehabilitation of the sick or injured is a continuous process"[1] which should end in satisfactory resettlement in industry. There is no clear-cut dividing-line between medical and industrial rehabilitation, and ideally there should be none between industrial rehabilitation and resettlement.

The function of rehabilitation has been described as "to restore the worker to industry, the citizen to society, and the man to himself,"[2] and to this end the services provided by the Ministry of Health and the Ministry of Labour and National Service play most important parts.

Throughout the war years the prevention and limitation of disability and invalidism and the refitting of those who had been out of work for considerable periods through physical disablement became matters of supreme importance. This task was shared by the Ministry of Health, which was responsible through the hospitals for the medical treatment and medical rehabilitation, and by the Ministry of Labour and National Service, which was responsible for resettlement in suitable work, including, where necessary, the provision of industrial rehabilitation, vocational guidance, and training. With the conclusion of the war the sense of urgency has been somewhat lost, and it is necessary to recognize that to-day, when full employment of both able-bodied and disabled persons is equally essential to the national economy, full use should be made of the facilities which are available for putting people back into productive work.

A paragraph in a Ministry of Health circular to regional hospital boards concludes with these words: "Every practitioner who has the care of serious and disabling complaints must assume responsibility for seeing his patients through to the point where they can either resume their former employment or be passed to the disablement resettlement officer of the Ministry of Labour and National Service (D.R.O.), for placing in some suitable alternative occupations. The responsibility for assessing disability and advising on residual capacity and suitable conditions of work belongs to the medical practitioner. The responsibility of placement in work rests with the D.R.O."[3]

This statement of policy by the Ministry of Health has not achieved the wide publicity and response which are its proper due, and in this article an attempt is made to illustrate one of the methods used by the Ministry of Labour and National Service to assist the doctor, be he specialist or general practitioner, to assume this additional medico-sociological responsibility.

Section 3 of the Disabled Persons (Employment) Act, 1944, requires the Minister of Labour and National Service to provide industrial rehabilitation courses for persons who are unable to work owing to unfitness due to injury, disease, or deformity, and who require these facilities to make them fit to return either to their previous employment or to other employment which is most suited to the altered capacity for work.[4] These facilities are provided by the Ministry of Labour and National Service in their industrial rehabilitation units (I.R.U.s), and in most cases follow on as a natural sequence to hospital or general-practitioner treatment services. Approximately 20,000 people have now passed through the I.R.U.s.

The first I.R.U. was set up at Egham, Surrey, at the beginning of 1944. This is a residential unit. Since 1948 13 other units (non-residential) have been set up at Birmingham, Bristol, Cardiff, Coventry, Edinburgh, Felling-on-Tyne, Glasgow, Hull, Leeds, Leicester, Long Eaton, Manchester, and Sheffield. There are places (available to both men and women) for 100 patients at each unit except Egham, which can take 200, and although the units are non-residential, with the exception of Egham and Leicester (50 residential places), suitable lodgings can be found near to the units.[5]

### Objects and Aims

These can be shortly summarized as: (1) To restore the fitness and confidence of persons suffering from physical or mental disabilities which handicap them in obtaining and keeping employment. (2) To discover by observations and tests and with medical advice (*a*) the personal factors which may be impeding satisfactory settlement in employment (there is abundant evidence that the importance of these factors is increasing daily), and (*b*) the types of employment most likely to lead to permanent settlement.

Most people after sickness or injury are able to return to their previous employment and the same job. Sometimes there is a permanent disability which makes a return to the previous job of work impossible, and in this type of case the assessment of the remaining ability in relation to future employment is essential if resettlement is to be permanent. It is amazing to find that, given the proper incentive, people can draw on their remaining abilities to achieve almost the same result in work effort as they obtained prior to the illness or injury.[6] There are, of course, obvious exceptions. It is assumed in all cases that the result will be *work*, usually of a permanent character, and it is a condition of entry to the industrial rehabilitation course "that the applicant will not only be fit for work at the end of the course but will have a reasonable chance of getting employment suited to his capacity."

### Availability of Courses

Any person aged 16 or over who has suffered illness or injury and is in need of industrial rehabilitation in order to get fit for work is eligible to apply for a course. These persons are divided into two main groups:

(1) Persons in this group are recommended on the completion of active medical treatment by consultants and specialists, hospitals, general practitioners, and industrial medical officers as being in need of a period of graduated hours of industrial activity before they can resume a full

day's employment. There are cases which also require vocational guidance for a new type of employment. There are no formalities in submitting the person for industrial rehabilitation—a simple recommendation by a doctor that his patient is in need of industrial rehabilitation is sufficient to enable the disablement resettlement officer (D.R.O.) of the local employment exchange to take the necessary action to have the application considered by the nearest I.R.U. At present 66% of the applications submitted come from hospitals and general practitioners in almost equal numbers: this percentage should grow considerably as the advantages to patient, doctor, and country are fully recognized.

(2) This group comprises unemployed persons, mostly disabled men and women who have been unemployed for some considerable time largely because they have not been able to obtain this particular kind of help when they needed it. Most of these cases are identified by the D.R.O.s from among persons attending at the local employment exchanges. It is the gaps between the phases of resettlement which are so damaging and soul-destroying, and the constant endeavour of the department is to make rehabilitation in all its phases a continuous process from the onset of medical treatment to employment or re-employment.

The applications are submitted to the units, who decide whether the cases will benefit from a course of industrial rehabilitation, having regard to all the circumstances. Very few cases are in fact rejected, because each unit has had experience of amazingly successful results in cases which seemed far beyond any assistance. The maximum length of the course is 12 weeks, but the usual period is from six to eight weeks. Maintenance allowances are paid according to the family circumstances. An analysis of the cases leaving three of these units is given in Table I. The age incidence of patients attending three of these units is shown in Table II. The

TABLE I.—*Analysis of 200 Cases Leaving Each of Three Units*

| | Surgical | Medical | Psychiatric | Others |
|---|---|---|---|---|
| Unit A .. .. | 22% | 51% | 20·5% | 6·5% |
| Unit B .. .. | 19% | 54% | 19% | 8% |
| Unit C .. .. | 25·5% | 55·5% | 10·5% | 8·5% |

TABLE II.—*Age Groups*

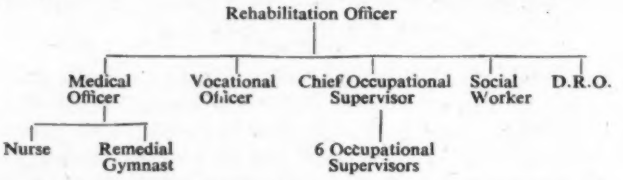
| | 17 and Under | 18–29 | 30–40 | 41–47 | 48–55 | 56 and Over |
|---|---|---|---|---|---|---|
| Unit A .. | — | 33·5% | 25·5% | 15·5% | 20% | 5·5% |
| Unit B .. | — | 36% | 28% | 16% | 16·5% | 3·5% |
| Unit C .. | 0·5% | 25% | 24·5% | 18·5% | 21·5% | 10% |

age group under 40 varies from 50% to 64% and age group 48 and over varies from 20% to 31.5%—that is, a considerable proportion of older people are benefiting from the courses. This proportion will rise as the liaison between hospitals, general practitioners, and unit is increased—a most important factor in the continued employment of the elderly.

### The I.R.U. and Its Staff

The facilities of I.R.U.s include a gymnasium, workshops, and gardens, and these are used as necessary to meet the needs of each individual undergoing a course. There is no standard curriculum, but an individual approach for each case. The workshops provide toning-up exercises on productive work as well as an opportunity to test vocational aptitudes and the ability to stand up to a full day's work. Outdoor work in the gardens and physical training in the gymnasium supplement workshop activities. Vocational training is not given during the course, but it may be given subsequently in a Government training centre, technical college, or an employer's establishment.

The actual working of the I.R.U. is the function of a team of specialists (see diagram) headed by the rehabilitation officer, who is chosen for his industrial experience and administrative ability and whose responsibility is to guide and co-ordinate the work of the whole team.




The medical officer attends on a sessional basis up to a maximum period of 15 hours a week. Each new entrant is examined as soon as possible after admission, and previous medical histories are usually available. The purpose of the initial medical examination is to: (*a*) diagnose the nature and extent of the disability (if any); (*b*) assess its effect on working capacity; (*c*) determine what, if any, toning up is necessary; and (*d*) decide whether, after any necessary toning up has been given, a return to pre-disability occupation is likely to be possible.

The medical officer provides the link between the unit and the medical agency which submitted the case. He is responsible for the work of the remedial gymnast, who, working in the well-equipped gymnasium (Fig. 1),

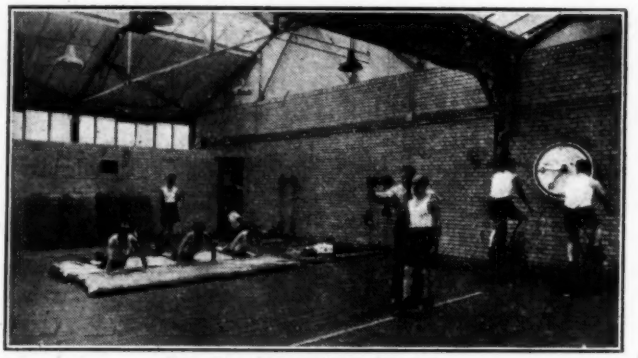


FIG. 1.—Gymnasium exercises.

arranges classes for the various types of disability. The remedial exercises in the workshops aim at correcting functional deficiencies or providing diversionary occupation (Fig. 2). It must be emphasized that at the earliest stage the atmosphere of productive work is introduced. There may be controversial opinions about the introduction of "work atmosphere" at the earliest stage, but the results obtained have justified this approach.

The functions of the nurse require no elaboration here; she is indispensable to the work of the medical officer.

The vocational officer is a trained psychologist whose special function is to discover in what particular direction lie the talents and aptitudes of those men and women who have to take up new employment and are in need of guidance on the kind of employment to seek. In vocational guidance the idea is to match the fundamental needs and the physical and mental capacities to a vocation, but it is a role that is rarely completely achieved. No man's vocational scheme of life can be separated from his total personality, and man has to be

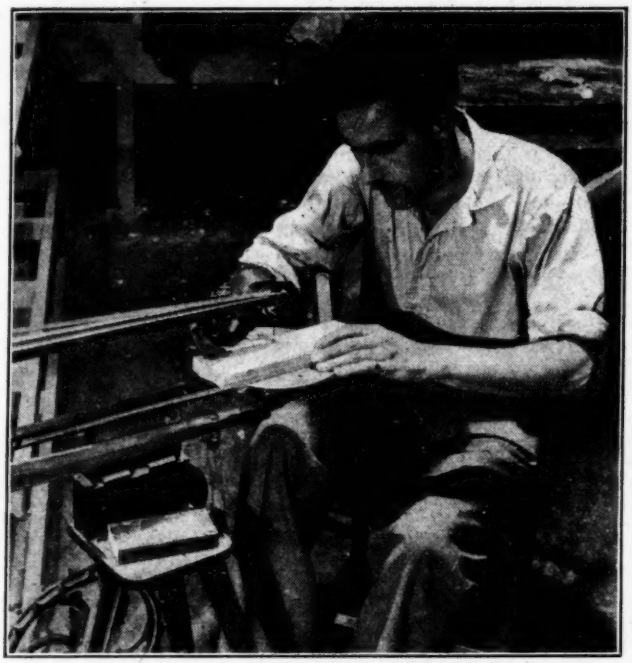


FIG. 2.—Working a treadle fretwork machine in order to learn accurate control of artificial arm.

considered in relation to this total environment, which to a very large extent conditions his total personality. The real test of a man's capacity is the actual performance under normal employment conditions or under a close simulation of them. This is a further reason why units tend to insist on the early introduction to normal employment conditions.

Occupational supervisors are in charge of the workshops and gardens and outdoor activities, and there is a social worker to assist with social, financial, and domestic difficulties which may be impeding progress and resettlement. The D.R.O. is mainly concerned with obtaining employment for those who need placing after their course of rehabilitation at the unit has been completed.

Although each member of the staff has his own distinctive contribution to make, it is only by their close collaboration as a team that the work can become fully effective. Each patient has his or her course carefully planned by the team in conference, and the succeeding stages are the result of team discussion. When the concluding stage of the course has been reached there is a "case conference" by the team, at which a recommendation is made regarding the most suitable type of employment that can be undertaken by the rehabilitee in his or her improved physical and mental state. *Over 80% of the persons who complete a course are found suitable employment or are placed in training courses which lead to employment.* In about 14% the recommendation is for vocational training in a skilled trade.

It has recently been recognized that workers of 56 upwards are capable of training up to a state of semi-skill if the job is sufficiently broken down. This is a definite advance on previous policy that it is unwise to attempt to train to any degree of skill after the age group 40–45.

Table III illustrates the success of the scheme.

The proportion of premature terminations may seem high, but it includes an appreciable number of persons who are automatically recorded as "terminations" after a period of two weeks' sick absence and who may subsequently return to the unit.

TABLE III.—*Cumulative Total of Entrants and Terminations from Date of Opening to April 30, 1951, and Number in Units at that Date*

| No. of Entrants | No. of Terminations | | | No. in Units at April 30, 1951 |
|---|---|---|---|---|
| | Completed Course and Recommended for Placing in Employment or Vocational Training | Premature Terminations | Total | |
| 21,771 | 17,327 | 3,272 | 20,599 | 1,172 |

## Conclusion

With the further co-operation of hospitals, consultants, and general practitioners, still greater progress will be made and a great preventive and social objective will be achieved—*the recognition of the tremendous productive potentialities present in every individual regardless of physical defect.*

The profession must accept its social responsibility in resettlement by the early "recognition of physical and mental defect" and by using all the available resources to achieve a successful return to work. Rehabilitation should be "the consummation of good work—not the salvaging of inferior," and, as truly stated by A. Miller,[2] "it should be judged by its social failures rather than by its medical successes." The I.R.U.s of the Ministry of Labour and National Service have achieved a large measure of success in the resettlement of disabled and potential disabled persons. The closer collaboration and co-operation of the medical profession with these units can largely aid in eliminating this social problem.

REFERENCES

[1]Brussels Treaty Permanent Commission Joint Committee on the Employment of the Disabled, June, 1950.
[2]Coal Board Conference on Rehabilitation, October, 1949.
[3]Ministry of Health Circular, RHB 49/36.
[4]Disabled Persons (Employment) Act, 1944. Section 3.
[5]*Ministry of Labour Gazette*, May, 1950.
[6]Kessler, H. H. (1947). *Rehabilitation of the Physically Handicapped.* New York.

## THE MAKING OF DEXTRAN

There are three possible types of substitute for human plasma in transfusion therapy: some other kind of protein (e.g., gelatin), a synthetic polymerized plastic (e.g., polyvinyl pyrrolidone), or a carbohydrate. So far protein substitutes have proved unsatisfactory, and, while one plastic ("plasmosan") is now commercially available as a 3.5% solution in standard transfusion bottles, by far the most highly developed group is that of the carbohydrates. Gum acacia has now finally been abandoned, but laminarin from seaweed is under trial, and dextran, a starch-like substance made by the bacterium *Leuconostoc*, is being widely tried out and has had considerable clinical approval (see p. 591). The dextran now being increasingly used in British hospitals is principally made by Dextran, Ltd., formed in 1949 as an offshoot of the East Anglia Chemical Company, Ltd., and the present factory at Darlington, producing 20,000 half-litres a month, has already given rise to another branch of similar size at Johannesburg (South Africa), and may soon be producing also in the United States. Apart from some work done in Sweden long-standing chemical research on dextran has been undertaken only in Britain. Its use as a plasma substitute has developed from the beginning through a unique association of Government, university, and commerce. The Medical Research Council, the Lister Institute, and the Colonial Products Research Council have been interested in the project from the start, and its development

followed directly from the comprehensive work undertaken for many years at Birmingham on carbohydrate chemistry under the late Sir Norman Haworth and Professor M. Stacey. This particular use of dextran was proposed by the Birmingham workers as far back as 1939, and both they and Sir John Simonsen (Director of Research, Colonial Products Research Council) have been interested in the commercial developments since 1943. Most of the scientific staff (16 at Darlington) have come from Birmingham University's school of organic chemistry or from its department of industrial fermentations. For a long time the term "industrial fermentation" has meant principally the brewing of beer and the manufacture of vinegar, but the coming of penicillin, streptomycin, and the newer antibiotics has greatly widened its importance, and the modern industrial microbiologist has to be a master of a curious mixture of industrial chemistry and medical technique.

In principle, the manufacture of dextran is simple. A solution of cane sugar (sucrose) with mineral salts, principally sodium ammonium phosphate, and added extract of fresh baker's yeast, is inoculated with a culture of *Leuconostoc mesenteroides* (betacoccus arabinosaceus strain) which is allowed to grow so that it makes dextran in the course of its life. Dextran is a bacterial starch composed, like ordinary starch, of glucose molecules linked in chains, but, whereas in ordinary starch the chains are mostly fairly straight, since the glucose units are linked end to end, in dextran they are coiled, since the pattern of linkage is different. There is no fixed molecular size at which the chain-making stops, and any culture will contain a whole range of sizes. For clinical use as a plasma protein substitute, however, only a medium size of molecule is suitable. The crude culture therefore requires depolymerization—i.e., breaking up of any large molecules, and the removal of any small ones.

The manufacture of dextran could be carried out on a small scale in any hospital laboratory, but continuous bulk manufacture introduces complications, chiefly the difficulty of maintaining asepsis throughout the process when dealing with large volumes of solutions and of maintaining a pure, vigorous, high-yielding strain of the living organism. All media are sterilized at 15 pounds per square inch steam pressure for 30 minutes at neutral *p*H. The precise conditions are very important, because if the cane sugar is hydrolysed (inverted) by the heating to glucose and fructose no dextran will be formed. Bacteriological testing and aseptic technique at important stages prevent the entry of pathogens or of bacterial contaminants which might produce other fermentations. Acetone is used to purify the dextran, and the final product is passed through Seitz filters into bottles which have been washed with detergent, rinsed in hot water, and baked for four hours at 170° C. to destroy pyrogens.

Numerous organisms produce dextran, but the particular strain used industrially has been chosen for its high yield and efficiency under convenient working conditions. Pure cultures of the strain are maintained in the laboratory on sucrose yeast-extract agar slants subcultured at 14-day intervals: each culture is incubated for three days at 23° C. and then stored at 4° C. For industrial use the quantity of growth is stepped up in three stages, through a three-litre culture and a 150-litre seeding vessel to the actual large stainless-steel principal fermenters. Each fresh volume of medium in the fermenter is newly inoculated in this way, and the fluid agitated to remove carbon dioxide and cooled to 25–27° C., as the heat of fermentation is great. Timing, seeding rate, temperature control, and medium composition are all important, and tests are constantly carried out on the viscosity, *p*H and titratable acidity, and dextran content of the medium as a guide to progress. 80% of the theoretical maximum of dextran from sucrose is obtained after 36 hours, and the fermentation is then arrested and the crude dextran depolymerized at once by a patented process. Fractionation to remove the unwanted very large and very small molecules is performed by adding different strengths of acetone–water mixture which precipitate different sizes of dextran molecule as judged by viscosity measurements, and the final remaining amount of low molecular weight material is estimated in rabbits by measuring the dextran appearing in the urine after intravenous injection. Salts are removed with anion and cation exchange resins (synthetic "water-softeners"), and other purifications follow. Each batch of finished product has to be tested for sterility, for toxicity to mice, for pyrogenicity and antigenicity to rabbits, and for anaphylactoid and cutaneous reactions in guinea-pigs. In addition the residual potassium content and chloride, the *p*H, and the viscosity are all measured or observed.

As well as its use in transfusions, dextran in certain other sizes of molecule as the sulphate is being developed as an anticoagulant. Raw dextran is also used in making ice-cream; and fructose, the principal by-product of dextran manufacture, is valuable to the confectionery trade.

## THE MAKING AND TAKING OF MEDICINES

### AN ANGLO-AMERICAN PRODUCTIVITY REPORT

The series of reports of productivity teams sent to the United States under the Anglo-American Council on Productivity to study American methods of production with a view to improving those in this country now includes one on the pharmaceutical industry which was published this week.[1] Unlike some of the other reports, this does not comment on the difference in diets and the consequent effect on the capacity of individual workers; the team do not consider that Americans work any harder, if as hard. To increase British production some suggestions are put forward. A "more generous attitude" on the part of Government departments in the import of machinery is urged, and among other points made is one that motion studies should be used to reduce unnecessary fatigue. It is stressed that "the highest productivity . . . can be approached by specialization in manufacture and by reducing wherever possible the range of products made."

It is clear that the American pharmaceutical industry operates under conditions very different from those prevailing in Britain, due in large part to the differing demands of American doctors. In America the percentage of prescriptions calling for "medical specialties"—branded preparations advertised to the medical profession but not to the lay public—is substantially higher than in Britain, as much in fact as 9 to 12 times (and possibly more, because the English figures on which the team base this conclusion refer to National Health prescriptions in 1949, before the Ministry circulars of this year). The American manufacturer, partly because of this tendency of American doctors to prescribe medical specialties, manufactures a smaller range of products than his British counterpart. With so high a proportion of medical specialties being ordered, it follows that the prescribing of standard products is correspondingly smaller. This the team found particularly true of the older drugs, and many of the preparations of vegetable drugs still used in Britain were rarely required in America. The demand for pills in America, as in this country, is diminishing. Soft gelatin capsules are used to approximately the same extent in both countries, but hard gelatin capsules are much more popular in America than in Britain, and their preparation and filling constitute an appreciable part of pharmaceutical industry. The report states that the use of multi-coloured capsules is becoming common, perhaps because manufacturers find that the American likes his medicines as well as his ties to be gay.

Competition in America is very keen. This is true not only of the selling effort and selling price but also of research. "The present rapid expansion of the pharmaceutical industry in America has resulted from, and is associated with, a very extensive research and development effort,"

[1] Productivity Team Report: *Pharmaceuticals*. Anglo-American Council on Productivity, 21, Tothill Street, S.W.1. Price 3s.

states the report. "The introduction of a clinically effective drug, particularly one with a wide range of uses, can quickly change the whole character of a firm's production. The most recent benefits to medicine and to the pharmaceutical industry in America resulting from the intensively competitive research carried out are perhaps best exemplified in the antibiotic field."

Prices in America are higher than in Britain. This must be due in part to the increased amounts spent on advertising and promotion. But it is perhaps also a reflection of a different social attitude, for the average American is prepared, or has become accustomed, to paying more for his medicines than had the average Englishman before the Health Service.

## INTERNATIONAL CONGRESS OF ANAESTHETISTS

The 26th Annual Congress of Anaesthetists, held this week, was described by Dr. I. W. Magill, one of its presidents, as the first occasion on which an international congress of anaesthetists of such magnitude had been held in London. It was a quarter of a century ago—in 1926—that the last similar function was held in Britain, when the International Anaesthesia Research Society organized a joint meeting with the Section of Anaesthetics of the British Medical Association at Nottingham. Participating in the present meeting were the International Society, the International College of Anaesthetists, the Association of Anaesthetists of Great Britain and Ireland, and the Section of Anaesthetics of the Royal Society of Medicine.

The congress opened on Monday. Sir John Anderson, inaugurating the commercial exhibition held in connexion with it at St. Pancras Town Hall, said it was fitting that this international conference should be held in Britain, a country which had contributed so much to the tremendous progress which had been made in the development of the new science and technique of anaesthesia. Dr. W. A. Low, who introduced Sir John, pointed out that anaesthesia was definitely established as a specialty, and he added that the time had come when there should be a pooling of knowledge so that there could be good and up-to-date anaesthesia in all parts of the world. Whatever international society was set up should be founded on a firm basis.

The congress was in honour of the late Dr. H. Edmund G. Boyle, and on Monday afternoon members and their ladies went to Dr. Boyle's old hospital, St. Bartholomew's, where in the Great Hall they were welcomed by Dr. C. Langton Hewer. Mr. A. Charles King described his display of historic apparatus; it included the first English gas–oxygen apparatus made by Dr. Boyle in 1916, after he had used the Gwathmey gas–oxygen–ether machine. Mr. King quoted from the *British Medical Journal* of 1915 (1, 766) the remark by Dr. Boyle that "it was an important point that patient and anaesthetist should not be strangers on the morning of the operation." At the first full session of the congress, in B.M.A. House, Dr. Magill outlined Dr. Boyle's career, including his introduction into this country of the Boyle–Davis gag. Dr. Harold R. Griffith, the other president of the congress, conveyed the greetings of the International Anaesthesia Research Society, and paid tribute to the late Dr. F. H. McMechan and to Mrs. McMechan, who was present and helped in the organization. He said that what was wanted now was not so much new methods as the better use of those available.

Dr. Charles W. Metz conveyed the greetings of the American Society of Anesthesiologists, whose history he sketched from the founding of the Long Island Society of Anesthetists in 1905.

During the week the congress has heard many scientific papers, and other events included a reception by the British Medical Association, at which guests were received by Sir Henry Cohen, and the unveiling of John Snow's tomb in Brompton Cemetery by Miss Una P. Snow, great-niece of Dr. Snow.

# Correspondence

### "War" and "Peace"

SIR,—The signatories to the letter under the above title, in your issue of August 11 (p. 363), may for all I know be as heroic as the Quaker non-combatants of the last war, but they must not be surprised if those who don't know them wonder whether the "strongest exception" they take to the action of the Central Medical War Committee should not be regarded as a weapon of the cold war. Man has been on the earth a comparatively short time, and has not yet outgrown his natural reflex for fight or flight. History has little support for the success of non-resistance. A watchful enemy, who is an excellent psychologist and is urged on by what amounts to a religious belief in his own brand of "exclusive salvation," would certainly utilize the "conciliatory" attitude displayed by their association for his own warlike ends.

Another war may well be averted by preparedness, but the eve of battle, which the writers seem to prefer for such action, would have a remarkably short twilight for the unready.—I am, etc.,

London, W.1. E. ROCK CARLING.

*** This correspondence is now closed.—ED., *B.M.J.*

### Ethics of Prefrontal Leucotomy

SIR,—As one who has previously written in your columns against the indiscriminate use of physical treatments in mental illness (March 2, 1946, p. 328), I would plead for a balanced, unprejudiced attitude. The golden mean is never popular with extremists in heated controversy, but such is the proper attitude to adopt when dealing with obscurely caused diseases which prove refractory to the older, well-established treatments.

Nobody pretends that leucotomy is an ideal form of therapy, but in certain malignant types of mental disease it is the best that can be done in our present state of knowledge. Allow me to quote one case as an illustration. This patient was a schizophrenic of 15 years' duration; she was hand fed, faulty in habits, and exhibited frequent phases of violence; for over 10 years she had been confined in a locked turbulent ward. A leucotomy was performed by Mr. Wylie McKissock three years ago, and now she has again found her place in society and is gainfully employed, to the great delight of her mother. No doubt her emotional faculties are not as deep as they would have been if a recovery had been effected by some other less drastic means, but until such is discovered we can justifiably resort to leucotomy in a case like this.

I sympathize with some of Dr. D. W. Winnicott's views (August 25, p. 496), but I would not go to the extreme of saying that leucotomy should never be performed in the psychoneuroses. It is an unfortunate fact that a proportion of certain types of psychoneuroses—e.g., the obsessional group—fail to be cured by the most expert psychotherapists, and it would be adopting a bigoted attitude to refuse operation in such cases.

Dr. Winnicott's principle that the human being has the right to suffer needs some clarification. The healthy human being knows that a certain amount of suffering is part and parcel of life and accepts what fate allocates to him with a resigned philosophy, but it is doubtful whether he would vociferously demand the right to suffer in and out of season. Moreover, when considering leucotomy we are not dealing with a healthy mind, but with a seriously disordered mind, and rights which may be appropriate for the former are not necessarily appropriate for the latter. A melancholic may demand the right to be burned at the stake because she is convinced that she is a wicked harmful witch, but we do not accord such a right. Finally, even if we were to accord some human beings an unlimited

right to suffer themselves, this surely must not be allowed to involve unpleasantness for others, who may by no means demand a right to suffer. We must face the fact that relatives and friends of psychoneurotics and psychotics do not display an enthusiasm to suffer as a result of the abnormal behaviour of these patients.—I am, etc.,

Basingstoke. I. ATKIN.

SIR,—I should like to agree with Dr. D. W. Winnicott's letter (August 25, p. 496) and those others who protest against the fantastic use of this operation. One hopes, as he says, that the result will truly shock medical opinion. Dr. Winnicott rightly says that "the fundamental principle for which we must fight is that the human being has the right to suffer." May I suggest that it is just as important that he should not be *made* to suffer, and that often unnecessarily and repeatedly?—I am, etc.,

London, N.W.4. A. L. ROWSON.

SIR,—Desperate cases require frontal leucotomy under strict safeguards, which so far do not exist. In the absence of such safeguards there is great probability that indications for frontal leucotomy and other shock techniques will be widening. Many colleagues are profoundly disturbed that we have entered into an era of violence in psychiatry. They may still have to recover sufficiently to register their fears and protests. It is to be feared that treatable cases will now be shocked into submission and unconsciousness. Hitherto it was our privilege to assist them in their recovery, which necessitated co-operation and full comprehension of the significance of their suffering.—I am, etc.,

London, W.1. M. J. MANNHEIM.

## The Mechanism of "Conversion"

SIR,—The article by Dr. William Sargant on "The Mechanism of Conversion" (August 11, p. 311) seems to me of the greatest importance, but so far comments on it have missed what to me is the essential point—viz., that "conversions" due to the pressure of external force are in every sense of the word "sincere." This cuts at the root of all deductions made by historians and liberal thinkers from the methods of judicial inquiry frequently used in totalitarian states and all other occasions on which force, torture, and similar methods are employed. It seems that we have been mistaken in thinking that the rack, the thumbscrew, and the ducking-stool can have produced only conversions which were not genuine, but that, in certain cases at any rate, these "confessions" were made in all sincerity. Moreover, fixed principles instilled in childhood can now be altered in adult life and with no reference at all to reason.

I wrote in 1949 (*Royal College of Science Journal*, **19**, 88), dealing with witchcraft trials in Europe, "However good the intention may have been at first, abuse of such a practice (that is, torture) is too obvious for further discussion to be necessary," It is evident now, from the work that Dr. Sargant has so ably summarized, that the danger of the abuse of these methods must have been more real than we had previously imagined and that many of the forcible retractions and recantations of the Middle Ages and later were "genuine" in the only sense in which the word can now be used. It is horrifying to think that methods universally condemned as useless as well as cruel have been shown to be so efficacious. Where are we to draw the line between terror produced by torture and by abreaction? Who are we to trust to do this? And who is to decide what new principles of conduct are to be instilled?—I am, etc.,

Liverpool. R. E. REWELL.

SIR,—The most competent article on "The Mechanism of Conversion" by Dr. William Sargant (August 11, p. 311) illuminates clearly a decision facing the junior psychiatrist to-day, which, when made, will affect the basis of any approach which he may make to his patient. Dr. Sargant gives a most thorough and brilliant hypothesis that the aetiology of mental disease has a physical basis, with the concept of normality being of man the socially self-adjusting machine. The aim of therapy is to readjust the sick individual to a sane environment.

From this standpoint the psycho-analysts, the analytical psychologists, and clinical psychiatrists of the dynamic school are "blind mouths" who induce therapeutic emotional reactions but whose doctrinaire views render the quotation above applicable. The philosophical views of Eckhart, Kierkegaarde, and Schweitzer are at the best a mistaken interpretation of an epiphenomenon. The whole of Western philosophy must be relegated to the shelves of fiction and only the causally related facts of natural science utilized in the practice of psychiatry.

In the present controversy about leucotomy fully divergent views are being expressed by people whose clinical experience is considerable. To the younger psychiatrist they seem to be spokesmen of two widely differing schools of thought, so opposed in fundamental issues that a person could transfer from one to the other only by a conversion mechanism as drastic as those described by Dr. Sargant in his article. The choice must be made now, that his basic training may neither instil into him a series of conditioned patterns difficult to inhibit nor on the other hand prevent the development of the all-important insight so vital to the analytic techniques.

In following the lead of a mechanistic school of dualism we must surely leave behind us the transference situation of Freud, Menninger, Alexander, and Glover, the meaningful objectivity of Fromm, and the I-Thou of Buber, for these all imply that behind the dispassionate scientific eye of the mechanist lies a personality which insists on bringing something of himself into the situation with the sick human machine which is being observed.

Having threaded our way so far, we must now wonder whether one machine can enter into relationship with another. And, lastly, is a machine still a machine when it knows it is a machine?—I am, etc.,

Killearn, Stirlingshire. J. L. CAMERON.

SIR,—Dr. William Sargant's article on "The Mechanism of Conversion" (August 11, p. 311), coming in the midst of the present controversy over leucotomy (August 25, p. 496), further demonstrates how radical is the schism in present-day medicine.

Dr. Sargant states that the human being can be understood by the methods of natural science, and that it is useful as a working hypothesis to regard man as a machine of a highly complex and distinctive type, perhaps even unique among possible machines, but not different in essence. This machine may go wrong. In that case it (the patient) is "ill." The doctor's task is then to re-service this machine to a state of satisfactory functional efficiency—i.e., smoothness and ease of adaptation to the environment. Methods of doing this are similar to giving one's radio set a knock when it goes "hysterical." The justification of this procedure, with man as with the wireless set, is that "it works"—as indeed it does, in a sense.

This is an instance of the positivism which, failing to realize its metaphysical assumptions or denying their importance, makes so plausible an appeal to science and practical needs, but has the paradoxical result of regression to barbarism. The long struggle of thinkers in recent times, from W. Dilthey to Heidegger and K. Jaspers, to show that we come to know and understand a man in a manner quite different from the way in which we discover facts and causal relations in the world of objects seems to be regarded along with psychopathology and "abstract" philosophy as no longer a fundamental concern. It would seem that such an attitude could hardly arise merely from the observation that there are certain analogies between calculating machines and brain functions. Dr. Sargant's complete hypothesis can be held, however tentatively, only if it seems not to do too great violence to one's experience of oneself and of others. If one experiences oneself as something essentially similar to a machine then indeed most of the statements of "abstract" philosophers correspond to no recognized reality in one's own existence and must seem senseless or unimportant.

One cannot refute an experience: one can only state the contrary in accord with one's own experience.—I am, etc.,

Glasgow. RONALD D. LAING.

SIR,—Surely other readers of the *British Medical Journal* besides myself must have been profoundly shocked by the article by Dr. William Sargant appearing under the above title in the *Journal* of August 11 (p. 311).

"Intellectual argument and moral exhortation, used as treatment . . . in the last century" (was it ever believed to be effectual?) "have been increasingly abandoned." "The nervous system of the patient," we are told, "is now much more likely to be subjected to a variety of insults, both psychological and physical, because then better results seem to be achieved." There follows a lurid description of the psycho-analysis of the wretched victim, who is placed on a couch daily, "and over the course of months or years" is subjected to this process, until "emotional storms mount and the patient becomes more and more sensitized to the analyst," etc. One would imagine that with such nerve-exhausting treatment carried on daily for years the psycho-analyst himself must have a strong mental constitution to enable him to retain his own mental balance. The variety of "insults" (a really good expression, this, for such "treatments"!) both psychological and physical is indeed sufficiently terrifying, ranging—on the physical side—from repeated electric convulsions and insulin (and other) shocks to the deliberate mutilation of parts of the brain itself. There comes the thought, Can it be right that any person should be placed so completely under the power of another as some of these patients are placed under the power of the so-called psychiatrist? He is no more infallible than the ordinary physician with the ordinary (non-mental) patient, but his mistakes can be far more serious in their results. That leucotomy is sometimes forced upon patients against their will, even in cases where volition and ability to give or withhold consent are unimpaired, was testified in a letter from the deputy medical superintendent of a mental hospital published in the *British Medical Journal* of July 12, 1947 (p. 72). I do not remember that this letter provoked any comment such as one would have expected; but, surely, it is a matter for the Board of Control to take up.

Dr. Sargant bases many of the modern methods of psychiatric treatment on the results obtained by Pavlov in experimental work on dogs, but has to admit that "many physiologists and psychiatrists dispute Pavlov's mechanistic interpretations." We would go further and ask by what reasoning can such experiments (incidentally involving much cruelty) be justified. In the brain and its functioning there is surely a vast difference between man and the lower animals; and to argue from the mental reactions of dogs who have been subjected to treatment deliberately undertaken for "breaking down" their nervous systems to the mental effects of severe stresses on human beings is almost certainly erroneous; and psychiatry based upon such reasoning should be regarded with suspicion.

In conclusion, it is worth noting that the whole of the lecture is couched in language which conceals a great deal from the ordinary intelligent but not specially psychologically trained medical man; it savours almost of esoteric jargon. Such terms as "abreaction," "abreactive," "conditioned patterns of behaviour," "conditioned dog," "positive conditioned," "negative conditioned," etc., occur many times. The lecturer is not immune from some of the misuse of terms so often met with in psychological literature, as, for instance, when he speaks of "severe psychiatric illness," where it is obvious he does not mean what the words should properly mean.

Before the claims made by psychiatrists can be accepted it is of the utmost importance that they should be able to produce evidence of the follow-up in all cases—including cases of E.C.T. and leucotomy—which is, so far, lamentably wanting. The carefully made findings of W. H. Gillespie on the value of E.C.T. seem to have been conveniently shelved by psychiatrists of to-day.—I am, etc.,

Folkestone. E. WEATHERHEAD.

## Mescaline and Schizophrenia

SIR,—Dr. W. Mayer-Gross in his lecture (August 11, p. 317) makes the following statement:

"Symptoms of mescaline intoxication have been compared to those of *schizophrenia*, but it is much more the strangeness experienced by the patient suffering from schizophrenia and the difficulties of describing what is happening in the two conditions which are similar. Many typical schizophrenic symptoms, especially in subacute and chronic states, are never seen in mescaline intoxication. Early psychotic phenomena in acute schizophrenia show certain analogues, especially in the field of hallucinations and other sense abnormalities." (p. 320.)

Surely it is wrong to compare subacute and chronic schizophrenic reactions with the laboratory observations of trained psychiatrists taking mescaline? It is very unlikely that the unheralded schizophrenic psychosis of indefinite duration in an unprepared victim and the experience of a voluntary mescal taker who knows what to expect and how long his ordeal will last would be exactly similar. The remarkable thing is that these acute reactions have so much in common. Subacute and chronic schizophrenia cannot be compared legitimately with acute mescal poisoning but should be compared with chronic mescaline intoxication. Very little is known about this condition. One of the few references is quoted in the same lecture, and reads:

"The use of the drug was, and probably still is, a problem for Christian missionaries, who insist that its regular intake leads to increasing laziness and impairment of will power." (p. 317.)

A lay person might well describe some chronic schizophrenics in this way.

May it not be, to use his own phrase, that "the strangeness experienced by the patient suffering from schizophrenia and the difficulties of describing what is happening in the the two conditions" constitute an essential similarity? Language is not designed to describe the weird world of the mescaline taker and the schizophrenic. Only very rarely is the latter willing or able to describe his experiences coherently. When he does, as in Henning's astonishing book *The Witnesses*, the world which he describes is more like that of the mescaline taker than any other.

In our opinion Dr. Mayer-Gross's objection that all the symptoms of schizophrenia are not found in acute mescaline poisoning is invalid. So far as we can judge from the not very extensive evidence available the effects of mescaline vary as much but not more than the symptoms of schizophrenia, which unhappily for the diagnostic difficulties of psychiatrists allow a wide range of variability. In addition we have been unable to find much information about the effect of different quantities of mescaline in the same subject, so that one cannot be sure that some of the variations in mescaline symptoms may not be due to different dose–body-weight ratios or different rates of absorption.

It remains to be seen what, if any, relationship exists between schizophrenia and mescal intoxication. The elucidation of this problem may prove to be one of the next great advances in psychiatry, but until more is known your readers should not assume that, widely experienced as he is, Dr. Mayer-Gross's views on this important topic are unchallenged.—We are, etc.,

London, W.1. HUMPHRY OSMOND.
JOHN SMYTHIES.

## Silicone in Syringe Lubrication

SIR,—Following the suggestion of Messrs. G. H. Darling and J. G. C. Spencer (February 10, p. 300), we have tried the use of silicone D.C.550 as a lubricant for our hospital syringe service. As a result of this trial we have found it unsatisfactory and have reverted to a modification of the usual liquid paraffin lubrication. The reasons for this failure may be of interest to others running a syringe service.

Apart from sterility, the one essential of a good syringe is that it should not leak. Many of the syringes in use in hospitals are not perfect in this respect. It is most exasperating to see air bubbling past the plunger while attempting to obtain 10 ml. of

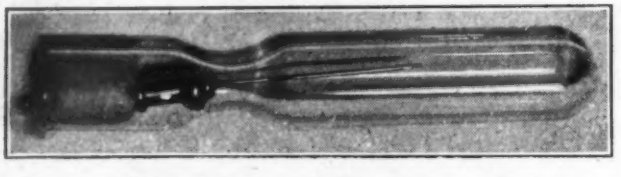
blood. To overcome this we applied more liquid paraffin. We obtained a good-fitting plunger, but when the syringes were sterilized any excess of liquid paraffin ran out and charred round the point of the needle. The use of silicone D.C.550 seemed to be the answer. The first results appeared to be very satisfactory: there was perfect contact between plunger and syringe and there was no charring. The difficulty arose when we attempted to clean the syringe, owing to the water-repellent properties of silicone. Darling and Spencer state that "the water-repellent properties of silicones make for easier cleaning after use." The direct opposite has been our experience. After boiling in soap and water the layer of silicone was not removed. Any deposit of hard soap and precipitated chalk stuck to this silicone layer (our laboratory has no water-still at present) and the syringes appeared "dirty" after washing. The silicone–hard-soap layer was partly removed during the drying of the syringe with acetone. The remainder was removed by the silicone–ether mixture, which very soon became cloudy, making frequent centrifuging necessary. All these cleaning procedures, however, considerably increased the time taken in preparing the syringes. The use of a water-softening agent ("calgon") added to the washing water prevented the deposit of hard soap, but even so the layer of silicone was soapy and still made the acetone and silicone–ether mixture cloudy. Another serious disadvantage of silicone D.C.550 is its high price. A 1-lb. bottle costs 48s., a phenomenal price compared with liquid paraffin.

We have now reverted to a modification of the liquid paraffin lubrication of syringes. For this we use a mixture of one part liquid paraffin and two parts ether. This mixture is placed for use in a wide-mouthed 25-ml. universal container (three-quarters filled). This is very convenient in use, as nearly all our syringe plungers (all-glass type) will dip into the container and the small-size neck prevents excessive evaporation of the ether. The plungers are placed in the mixture to three-quarters of their length and allowed to drain rapidly. By this method we can achieve perfect contact over the whole plunger area. The amount of liquid paraffin is not excessive and none runs from the end of the needles; there is no charring unless the oven temperature exceeds 180° C. Our syringes are sterilized in glass containers for 1½ hours in a hot-air oven at 165° C., this temperature being that taken at the rack level. The temperature at the top of the oven (where the usual thermometer is situated) is somewhere in the region of 200° C.—I am, etc.,

London, N.15. McD. DUXBURY.

## Sterilization of Hypodermic Needles

SIR,—It has always been difficult to keep hypodermic needles sharp through the process of sterilization. The difficulty arises that needles which have been sterilized by boiling cannot easily be stored, and consequently they are repeatedly boiled and quickly blunted. The waisted test-tube as shown in the accompanying photograph was introduced into our anaesthetic department two years ago from the Wesley Hospital, Chicago, U.S.A. The needles with their cotton-wool stoppers are placed in these test-tubes



and autoclaved at 15 lb. per square inch pressure, temperature 250° F. (121° C.) for 30 minutes, and we have found that they will remain sterile for at least 12 months without any attention, so that sterile needles are readily obtainable at any time. In order to facilitate storage in the anaesthetic rooms and make them easily accessible a plastic stand was made by the instrument department of this hospital to carry thiopentone and an assortment of needles. These needles can be replenished from stock as required, and consequently sterile sharp needles are always available to the anaesthetist.—I am, etc.,

London Hospital, E.1. S. D. K. STRIDE.

## Rupture of the Spleen

SIR,—I have read with great interest the paper on the surgery of the spleen by Sir James Learmonth (July 14, p. 67). I note that I have been more fortunate than him in one respect: I have personally performed splenectomy on *three* cases of injury to the spleen. As each case was different, I feel that therefore three and not two groups of injury to the spleen (other than blast injuries) exist. Brief summaries of my three cases are as follows:

*Case 1.*—A girl aged 14 was brought to hospital at about 11 p.m., having been knocked down by a car. There was no external bruising nor any physical signs of injury. As she was in a highly hysterical state (having been out walking without her mother's knowledge and consent) it was decided to keep her overnight. At about 5 a.m. the night sister informed me that the patient had suddenly collapsed and seemed on the point of death. When seen by me she was pale, cold, and with a pulse rate of 120 per minute. Blood and oxygen were given at once and a laparotomy performed as soon as she was in a fit state. About 2½ pints (1.4 l.) of blood was in the peritoneal cavity and a ruptured spleen was removed. Four pints (2.25 l.) of blood was given in the 24 hours following her collapse, and her recovery was quite uneventful. It is interesting to note that the police informed me that the car was deeply dented at the point of impact. The spleen removed was about three times the normal size (but with a normal histology), and it was torn almost completely across about its middle. It was not adherent to the diaphragm.

*Case 2.*—A boy aged 16 was admitted late at night on a Sunday, having fallen off his bicycle. No physical signs of injury were present on admission. The next day he complained of slight nausea and on Tuesday had a little pyrexia. His pulse gradually rose to 110 a minute by Thursday, and it was decided to perform a laparotomy with a provisional diagnosis of ruptured spleen. At operation a small amount of blood (not more than ½ pint (284 ml.) was in the peritoneal cavity, and a spleen with a large subcapsular haematoma was removed. No blood was given and recovery was quite uneventful. The spleen was about twice normal size (but with a normal histology), but its capsule was firmly attached to the diaphragm. The substance of the spleen proper was not torn.

*Case 3.*—A man aged 35 was admitted one evening at about 6 p.m. with the history of having fallen off his bicycle the previous evening. He was able to go home by himself, but spent a restless night because of pain in the abdomen, and next day had severe vomiting. When seen by me he was pale, his pulse was 132 per minute, and he had shifting dullness. At an emergency laparotomy some 2 pints (1.1 l.) of blood was found in the peritoneal cavity. The spleen was small and firmly adherent to the diaphragm by multiple adhesions. The bleeding was found to come from a vessel at the hilum. Splenectomy was performed (and was rather difficult). No blood was available for transfusion until the next day, but the patient recovered after a rather stormy convalescence.

On the basis of these three cases I feel that the groups of injury to the spleen are (1) large non-adherent spleen = rupture of the substance of the spleen; (2) large adherent spleen = subcapsular haematoma with leak or delayed rupture into peritoneal cavity; and (3) normal-sized adherent spleen = tear of the hilar leash of vessels.

I was in fact preparing a communication on ruptured spleen on the above lines, but this is difficult here, as no adequate reference library is available.—I am, etc.,

Georgetown, British Guiana. N. N. IOVETZ-TERESHCHENKO.

## Aspiration Lung Biopsy

SIR,—In connexion with the description of the technique of aspiration lung biopsy used by Drs. Philip Ellman and Alexander Gee in the study of "Pulmonary Haemosiderosis" (August 18, p. 384) a reference was made to the technique applied by me (*J. clin. Path.*, 1949, **2**, 49). I believe the authors misunderstood the intention of the "two-needles method" used in lung biopsy. My original paragraph reads: "The precaution of using the two-needle method in lung biopsy was necessary only for identification of certain cells and exclusion of cellular elements of the pleura and skin. For ordinary diagnostic purposes the one-needle method is entirely satisfactory if it is kept in mind that the cells described below belong to the serosa of the pleura."

I would like also to take this opportunity to stress the following points in the technique of aspiration lung biopsy:

In order to avoid an undesirable reaction of vaso-vagal syncope resulting from puncture of the parietal and visceral pleurae and of the lung tissue itself a thorough infiltration with 2% solution of procaine (or its equivalent) of the area of both pleurae and adjacent lung through which the needle will penetrate is essential.

Pneumothorax results from the needle biopsy only very rarely; it is then usually of minor degree and causes little or no distress to the patient.

The danger of a major haemorrhage is substantially minimized if aspiration is carried out under *x*-ray control and the needle used for the biopsy is of the lumbar type with a small bore. It should have a short bevel and the stylet should be in place during insertion of the needle.

Aspiration lung biopsy should be applied in selected cases of lung disease where the diagnosis cannot confidently be made.—I am, etc.,

Edinburgh. Z. Z. GODLOWSKI.

## Ascaris in Common Bile Duct

SIR,—The case recorded by Mr. E. H. R. Altounyan of ascaris or roundworm impacted in the common bile duct (August 11, p. 338) recalls a similarly interesting case operated upon by the late Sir Hugh Rigby at the London Hospital (*Brit. J. Surg.*, 1923, **10**, 419).

The patient, a woman aged 30, was admitted as an abdominal emergency, and at operation was found to be suffering from acute haemorrhagic pancreatitis. There was much reddish fluid in the abdominal cavity, multiple fat necroses of the omentum and mesentery, and the pancreas was much swollen, maroon-coloured, mottled on the surface, soft, and sponge-like: there was no obvious sign of disease in the gall-bladder or bile ducts. The lesser sac and pelvic cavity were drained, but the patient did not rally and died the following day.

The condition found at necropsy showed "part of a roundworm projecting through the sphincter of the common bile duct, the body passing through the duct of Wirsung and turning into the duct of Santorini, so that both ducts were effectively blocked. There was bile staining of the terminal inch of the duct of Wirsung, and dilatation of the common bile duct was present, though bile could easily be expressed from the gall-bladder into the duodenum."

In the same number (p. 421) of the *British Journal of Surgery* in which Sir Hugh's case appeared there is a further case recorded by another "Old Londoner," Lieut.-Colonel Novis, of the I.M.S., Bombay. Here the patient, a Hindu girl aged 12, had been suffering from recurring attacks of severe abdominal pain, and at operation a greatly enlarged pancreas was exposed between the stomach and transverse colon.

The stomach, gall-bladder, and bile passages were normal to palpation. An incision, which extended from the head of the pancreas to the tail, was made, extending down to and opening the pancreatic duct, from which a full-sized roundworm and a partially disintegrated one were extracted. The incision in the pancreas was united with interrupted catgut sutures and the abdomen closed, leaving a soft rubber cigarette drain down to the pancreas. During convalescence several roundworms were passed after administration of santonin, and the patient was discharged 23 days after operation, fat and well.

—I am, etc.,

London, W.1. MICHAEL SMYTH.

## A.C.T.H. and Pulmonary Tuberculosis

SIR,—During the recent conference at Oxford on tuberculosis and diseases of the chest, I referred to the use of A.C.T.H. in a patient suffering from pulmonary tuberculosis, and this was reported in the summary of my remarks in your issue of August 4 (p. 296). It has been shown experimentally that the effect of tuberculosis in animals may be enhanced by the use of cortisone (Hart, P. D'Arcy, and Rees, R. J. W., *Lancet*, 1950, **2**, 391; Spain, D. M., and Molomut, N., *Amer. Rev. Tuberc.*, 1950, **62**, 337), and there is also evidence that A.C.T.H. and cortisone may exert a deleterious effect upon tuberculous lesions in humans. The Committee on Medical Research of the American Trudeau Society issued the following statement at the end of 1950.

. . . Because the action of A.C.T.H. and cortisone upon the factors of resistance to tuberculosis has been shown to be deleterious in at least three species of experimental animals (mice, guinea-pigs, and rabbits) and there is strongly suggestive evidence along the same lines in human beings, it is recommended that these substances should *not* be used in patients with active tuberculosis, and that they be used with extreme caution even in human beings with possibly latent tuberculous infection, until such time as further investigative work has shown that such administration may be safe. The routine diagnostic examination for tuberculosis of patients under physicians' care is especially necessary for patients who are being considered for A.C.T.H. or cortisone therapy. . . .

As I have received a number of inquiries concerning the technique employed in the case which I referred to at Oxford, I wish to reiterate the need for extreme caution in the use of these substances in the presence of tuberculosis and to emphasize again that the case in which I have tentatively used A.C.T.H. is an exceptional one, and that, although the specific effect for which the substance was given—i.e., to overcome streptomycin intolerance—has been achieved, the overall effect of the treatment has yet to be fully assessed. I have certainly not thought it advisable to repeat the procedure in a second case until it is quite clear that no adverse effects have followed its preliminary use in one case. I would add that all laboratory facilities for the assessment of possible side-effects should be available if these drugs are used in tuberculosis.—I am, etc.,

Harefield, Middlesex. L. E. HOUGHTON.

## Experimental Exophthalmos and Cortisone

SIR,—In their paper on "Thyrotoxicosis and Radioactive Iodine" (August 18, p. 373) Drs. G. W. Blomfield, J. C. Jones, A. G. Macgregor, H. Miller, and Professor E. J. Wayne comment on a case of thyrotoxicosis with relative suprarenal cortical insufficiency, and on a case of malignant exophthalmos. I should like to refer to some preliminary experimental findings of mine which I consider to have a bearing on these problems.

Experimental exophthalmos has hitherto been produced mostly by crude anterior pituitary extracts. Since at least one of the factors responsible for the protrusion of the eyeballs is a change in the state of the retrobulbar connective tissues it was thought to be of interest to see what effect cortisone would have on this change. The degree of exophthalmos can be measured fairly accurately in the guinea-pig (see E. E. Pochin, "Exophthalmos in Guinea-pigs Injected with Pituitary Extracts," *Clin. Sci.*, 1944, **5**, 75). Thyrotropin, lot No. 50P5 (Parke, Davis & Co.), was therefore given to guinea-pigs, some of which received also cortisone ("cortone," Merck) before and during the period of administration of thyrotropin. Whereas a moderate degree of protrusion of the eyeballs could be produced by thyrotropin alone, exophthalmos appeared to develop more rapidly and seemed more marked in the cortisone-treated animals. The effect of cortisone on the course of thyrotropin-induced thyrotoxicosis is now being studied, since preliminary findings suggest that cortisone can affect the rate of loss of weight. It is hoped to publish the histological findings and details of the measurements at a later date.—I am, etc.,

Birmingham. K. ATERMAN.

## Failure in Examinations

SIR,—Mr. T. R. Henn (August 25, p. 461) discusses the conditions of stress in examinations and makes a comparison between staff college and university methods. I also passed staff college in 1942, and since 1946 have been an undergraduate. I have found it interesting to consider the reactions under these two methods of study, and believe that the reason why there is less tension at staff college than at university is because in the former course there is no formal terminal examinations, whereas in the latter "the examination" tends to loom too much on the students' horizon.

At staff college, as Mr. Henn says, the officer is surrounded by an atmosphere of stress, but it is also important to note that he is also trained to face up to such exigencies. Artificially produced stress is related to practical reality—*vide* the telephone battles and little sleep. The student is thus acclimatized to an atmosphere of realistic stress over a period of several months; he is assessed over a period of time by directing staff who live, work, and share the same stress. He is not passed or failed on the result of some 18 hours of high-pressure writing. Many of the syndicate exercises are exacting, but frequently syndicate libraries are available for reference, and efforts of memory are not expected. The student after a while acts naturally; he gives of his best not because he is keyed up and conscious that he must do so, but because he seeks to conquer the problems set rather than the examiner.

In the terminal "crisis" examination there is a concentrated effort with an associated physical strain and demand on memory. The student is very much aware of the test and consciously is aware of the demand to give of his best. In this condition he is more vulnerable to a trivial upset which would pass unnoticed in a real emergency where there would not be the existing tension.

Unlike Mr. Henn, I was impressed by the manner in which the regular officers faced up to the staff course. They took the course more seriously, but their enthusiasm and calmness were noticeable. I concluded that their greater interest helped them to overcome the tendency to "flap," since they were able to enter more whole-heartedly into the spirit of the course. Where interest was lost men thought of themselves rather than the task, and stress became apparent; men were then more likely to "flap" if called upon to take some responsibility.

The medical student is fortunate to have unlimited opportunity for clinical experience in the wards, and there is considerable stimulus for his interest. His chief problem is that he must learn the technique of answering the written paper under the present examination system. The more he can practise to write down his ideas the greater will be his confidence; but when it comes to the testing day he must have faith that he will not have toothache or have been up the previous night nursing the baby, or any other disturbing emergency which might make him knock over the hurdle instead of clearing it with ease.—I am, etc.,

Bromley, Kent. J. D. HARTE.

SIR,—Congratulations on having produced a really interesting Educational Number. Mr. T. R. Henn's article (August 25, p. 461) will prove most valuable to all doctors who have any responsibility for embryo students, whether medical or otherwise. It is a factual description and discussion of the cases which come before a tutor at one of the senior universities, but does it apply to medical students? Personally I have heard about these "flaps" from students at the senior universities, but in a long experience in a provincial city (from entrance scholar at the local grammar school to professor at the provincial university) I have never seen a student funk an examination in the way described, though I have once seen a mental black-out at a final viva.

The concise but vivid description given by Mr. Henn under the heads of strain of examinations and attitude to examinations is certainly true and serves to draw attention to what is one of the difficulties of our present educational system. The fact is that the reputation of a modern grammar or secondary school depends on the number of scholarships it obtains at the senior universities, and, since these scholarships are frequently classical, the obvious result is that the school will encourage the best intellects to classical studies. Under the emotional conditions described by Mr. Henn the pupil succeeds in getting to (say) Cambridge. He has a fine natural intellect, and if he mixes well with his fellows he soon finds that the classics are not the only matters worthy of serious study and that some other subjects may be of greater importance. He also finds that he himself is in a trap. If he can get a first, then the university career is open, but if he gets a second, then the only career possible is that of a schoolmaster, and even there lack of a first is an absolute bar to the good jobs. The glittering prizes of medicine, biology, physics, etc., are out of his reach. He loses the incentive which is necessary to most of us, and no wonder that he flaps. The classical scholarship man is thus forced by circumstances into a groove, just as is the case with the son of a doctor who has been forced into medicine to take over his father's practice—and we all know him.

Perhaps an even worse result of the classical scholarship system is that medicine, science, and engineering have had in the past to put up with the second-class output of the grammar schools—to the detriment of the nation. In medicine the question of a first was of little import apart from academical appointments, and even there it must be very rare for its possession to settle the question. Medical faculties know how easy it is for a first to rest on his laurels. When I retired five years ago there were suggestions that the schoolmasters were beginning to cram for the medical entries, and perhaps by now there are flaps before the preclinical examinations. Here again the medical student is fortunate. We have the Conjoint, the Halls, and the Triple. They are well worth keeping in reserve.

Mr. Henn's picture is sadly true for many students. It agrees with an account given to me by a most successful classical master of the nemesis threatening "coached" boys, especially in the classics. It should be read by all family doctors who have to advise the parents of bright boys.

If, Sir, you can bear with even more, may I give two practical tips? My father, not a doctor, under considerable financial strain (though I did not know it), about a fortnight before my final told me that, as he would have to stand the cost of failure, I was to go away for ten days' holiday without books. In fine physical form and with a due sense of irresponsibility I enjoyed the examination and just scraped through. The lesson was not lost on me when a parent myself. The second one is that, when faced with a failure in the final, it is a good plan to try for the next qualifying examination such as the Conjoint, even on borrowed money, then go as a temporary assistant into an industrial practice, pay off the loan, and return to the school *immediately*.—I am, etc.,

Helensburgh, Dunbartonshire. A. E. BARNES.

## The Full-time Consultant

SIR,—I wonder how many consultants holding full-time clinical appointments can parallel Dr. F. Avery Jones's experience (August 25, p. 443) that it is entirely feasible to graft research activities on to their routine work? My own much more junior and admittedly short experience has been the exact reverse—namely, an immersion in routine work so complete as to make research impossible, and even routine teaching difficult. Which experience is the norm?

There is, of course, no ideal ratio of routine to original work—it is a matter for individual compromise; and the striking of a balance which suits one's temperament and capacity is surely essential to the enjoyment of all consulting work, whether whole- or part-time. In this, however, the whole-time consultant is very much at the mercy of the regional board; and the view that every consultant should have some contact, however humble, with the frontiers of knowledge may be a difficult one to propagate, especially in times of financial stringency. It is understandable that a significant degree of detachment from day-to-day duties should tend to be allowed only to men who are senior and have an established reputation for teaching or research. But even a man of Dr. Avery Jones's standing, we learn, has to write most of his papers while on holiday, and he has to ask for better recognition of the principle of short periods away from routine work to enable senior men "to maintain their special studies in good perspective." Many would be glad of similar short periods in order to have special studies, without worrying too much about the perspective.

Whole-time consulting offers in principle a highly satisfying way of life, and Dr. Jones has obviously been able to approach very close to the ideal: my feeling, however, is that the average young consultant taking up a similar post and hoping to achieve a similar degree of professional freedom is likely to be disappointed.—I am, etc.,

Dunecht, Aberdeenshire. N. G. C. HENDRY.

### Higher Qualifications and Distinction Awards

SIR,—The deliberations of the Distinction Awards Committee appear to be completely secret; and one can only guess at the factors that influence the granting or withholding of an award. But it seems reasonable to suppose that, other things being equal, a Fellowship is likely to be regarded as more important than a Membership. I am impelled to write because under the heading "Higher Qualifications" (*British Medical Journal*, August 25, p. 491). it is said that, "The Royal College of Physicians of London confers its Membership . . . by examination. . . . Fellowship of the College is subject to election by the Fellows." This sounds as if the procedure is equitable and democratic; but the position is very different. Thus, as I am informed, Fellows are annually asked to nominate Members for the Fellowship. Then these names are placed before a council which weeds out the names of those it for some reason does not wish to be elected: the other names are then submitted to the comitia, which "elects." I am quite prepared to be told that I have made mistakes in my description of the procedure, but, by and large, it is correct.

Now, in the past, the possession of an F.R.C.P. was an honour highly prized by those to whom it was awarded, and earnestly sought by many Members of the College; but failure to obtain it did not really affect a physician's income. To-day, with distinction awards as an important part of many physicians' incomes, the absence of an F.R.C.P. may mean the difference between financial worry and financial security.

Is it then fair (perhaps a better word than the much abused "democratic") that the Royal College of Physicians should be run in this hole-and-corner way? It would seem only equitable that Members, as well as Fellows, should be able to send forward nominations; but—even more important—there should be no *Femgericht* to stop names from reaching the comitia of the College. Let the whole thing be open, and let individual Members have the right to bring their claims before the College as a whole, asking for such support from other Members and Fellows as they may think suitable.

An alternative would of course be to have an examination for the Fellowship, but there are too many examinations already; and the fact that examiners' meetings are *in camera* would still leave room for the machinations of a *Femgericht*.

I am not suggesting that all Fellows and all Members of the Royal College of Physicians should take part in the election of new Fellows: I should be perfectly content if the Fellows alone decided who was to join their ranks. But *all* the names proposed should be before them, not only those that have passed through the authoritarian net of the president's council—and why should not the voting be published, at least by being placed on the College notice-board?

It is for fear of diminishing the size of the mesh so much that I shall never be allowed to pass through it that I ask you to permit me to use the nom-de-guerre

DUM SPIRO SPERO.

### Smell of Coal Gas

SIR,—Dr. J. D. O'M. Poole (August 4, p. 302) suggests that coal gas should be irritant enough to awaken a sleeper, and it might rule out gassing as a means of suicide—he also refers to the law.

The law says that town's gas shall have the characteristic smell of coal gas—but it is impossible to describe a smell. Other domestic gas used, such as "calor" gas, is butane or butylene and does not smell of coal gas. It is essential that any odour given to gas must be quite unmistakable to the general public. In order to add an ingredient irritant enough to awaken a sleeping person, one has to ensure that the products of combustion of such an irritant are themselves not excessively irritant or corrosive. Such a noxious gas as visualized would almost certainly cause a great deal of upper respiratory tract irritation to the housewife, cook, and domestic user, to say nothing of the inconvenience and suffering to the manufacturers, distributors, and fitters. Gas-fitters constantly inhale small quantities of gas on revenue and maintenance work, but considerably larger quantities when called to mend a leak or burst main. Might not the inhalation of such an irritant over a number of years cause some permanent chest disability such as chronic bronchitis?

The poisonous element of coal gas (carbon monoxide) has been extracted experimentally, but it would be far too costly to do this generally. This is a subject which has been extensively studied and is constantly under review by the research chemists within the gas industry, and, although the addition of irritant substances might be desirable, it is not at present practical.

It is the duty of any consumer to make sure that the taps of all gas appliances are turned off when not in use, and there is also a day and night service always available to deal with leaks or escapes of gas. Admittedly the suicide rate from town's gas is high, but if gas were made to smell worse I doubt whether there would be a reduction in the annual suicide rate, as it is only one of many ways of committing suicide.—I am, etc.,

North Thames Gas Board. F. G. HOLMAN, Medical Officer.

## POINTS FROM LETTERS

### Dental Anaesthetics

Dr. A. C. M. COXON (Abingdon) writes: . . . The term "whiff of gas" (see July 28, p. 239, and June 9, p. 1314) means to me that the patient is not fully anaesthetized. If in this state teeth are extracted one must expect protests in varying degrees. . . . If gas must be given to one of robust and doubtful behaviour, use a strap. . . . I do my impactions and difficult extractions with local analgesia, and if a general anaesthesia is necessary, either from the sepsis present or the wish of the patient, then I use intratracheal ether and oxygen for difficult cases. I am not a "gas fan." I prefer local analgesia, but I have had considerable experience . . . my cases run into several thousands, and I state that gas has a very definite use in dentistry.

### Unnecessary X-ray Examinations

Dr. W. A. BELLAMY (Aylesbury) writes: A patient of mine went back to her home town to have her third baby in hospital, owing to lack of domestic help. Her two previous confinements were normal. I had attended her up to the eighth month and all was well. I got the hospital report, which included a number of *x*-ray examinations. I am informed that this is often the procedure, on primiparae and multiparae alike.

Desperately ill cases of pneumonia, admitted to hospital due to lack of home nursing, are, as a routine, repeatedly *x*-rayed. Surely the present-day obstetrician is not so barren of clinical acumen that all these *x*-ray examinations have to be done on normal cases. Surely the present-day clinician can follow pneumonia cases with his eyes and ears, without *x*-raying all of them. Or is the art of medicine leaving us, and only the science remaining?

### Antihistamines and Burns

Dr. M. M. KESSLER (North Arlington, New Jersey) writes: I was very much interested in the letter "Antihistaminics and Burns" (July 14, p. 117). I have had similar experiences using the same drug, and wrote an article on this subject which appeared in the January, 1951, issue of *Industrial Medicine and Surgery*. The findings are identical with those reported by Drs. Milne, Balfour, and Yeoman. We are continuing our work.

### The Dysenteries

Dr. M. ABDULLA (Vaniyambadi, South India) writes to draw attention to an ambiguity in the article by Brigadier J. S. K. Boyd (June 23, p. 1440), who states: "Emetine remains the favoured specific. In active infections three to five daily doses of 1 gr. (65 mg.) given subcutaneously will relieve the acute symptoms." This should be understood to mean doses of 1 gr. daily for three to five days, and *not* that up to 5 gr. can be given daily, as this would be a dangerous dose.

# Obituary

## A. GEOFFREY EVANS, M.D., F.R.C.P.

Dr. Geoffrey Evans, consulting physician to St. Bartholomew's Hospital, died suddenly on August 30 at his country home at Clifton-on-Teme, Worcestershire. He was 64 years of age.

Arthur Geoffrey Evans was born in 1886, the son of the late Patrick F. Evans, recorder of Newcastle-under-Lyme. From Charterhouse School he went on to Trinity College, Cambridge, with an exhibition. After taking a first-class in both parts of the natural sciences tripos he entered the medical school of St. Bartholomew's Hospital in 1909 with a senior science scholarship. He qualified in 1912, graduating M.B., B.Ch. in 1914, and proceeding M.D. in 1921. Among the many prizes and honours he obtained were the Brackenbury Medical Scholarship in 1912, the Laurence Research Scholarship in 1914, and the Horton-Smith Prize of the University of Cambridge in 1921. He became a member of the Royal College of Physicians in 1914 and a Fellow in 1922. At the College he gave the Goulstonian Lecture in 1923 and the Lumleian Lecture in 1943. He served for a term as president of the Section of Medicine of the Royal Society of Medicine.

At St. Bartholomew's Hospital Evans's career was outstanding. He was successively appointed assistant director of the medical unit, assistant physician, and finally physician to the hospital. His professional reputation was very high, and he became an accepted authority on the subjects of vascular disease, hypertension, and disorders of the kidney. With the late Sir William Girling Ball he was co-author of *Diseases of the Kidney*, and he contributed articles to several well-known textbooks of medicine.

In 1923 Evans was secretary of the Section of Medicine at the Annual Meeting of the B.M.A., and he became chairman of the St. Pancras Division of the Association two years later. A member of the Medical Planning Commission, he also served for a short time on the Consultants and Specialists Committee.

During the first world war Evans served as a temporary surgeon lieutenant in the Royal Navy from 1914–19. In 1917 he married the Hon. Ermine Mary Kyffin Taylor. There were four children of the marriage.

We are indebted to Dr. Geoffrey Bourne for the following appreciation: Dr. Geoffrey Evans's personality was exceptional. It was strong, vigorous, and extremely individualistic, but always tempered with a broad sense of humour and a fundamental kindliness. He loved the dramatic, and many of his teaching aphorisms gained their value from this quality, which impressed them indelibly upon his hearers. He was an extremely loyal servant of his hospital, and his professional ideals had the same sincere quality of true humanitarian service. His mental and physical vigour and activity helped him to get through an enormous amount of work, and his flair for organization enabled this to be done with thoroughness. Such was his vitality that his sudden death seems hardly believable to those who had met him just a few days before this event. His individualistic point of view, combined with his love of his profession and his sense of the necessity for professional freedom, made him a vigorous opponent of the Health Service as at present constituted. Nobody, however, could ever attribute to him motives which were not completely disinterested and honest. His passing will be much regretted and deeply mourned by those who knew and valued his personal qualities.

R. M. V. writes: To his friends the sudden death of Geoffrey Evans has caused the deepest distress. He has been stricken down while still in active practice—full of energy and looking forward to many years of useful work followed by a busy retirement at his home in the country.

Those of us who knew him well have our memories of his arrival at Bart's from Cambridge—an enthusiastic and brilliant student, marked down even in those days for rapid advancement. He lived up to our expectations. As time passed, he moved steadily upwards in his particular walks of life. At Bart's, to whose interests he devoted so large a part of his professional life, he went up the ladder of promotion, and ultimately became a consulting physician just after the appointed day. His memory will live in the hearts of many generations of Bart's men as a skilled physician and a most incisive and humorous teacher. In consulting practice he made his mark. He never spared himself in the investigation and treatment of his patients. His long clinical notes on each and all of them were a model of precision. Many doctors will remember with gratitude his unstinted help to them in difficult cases. He held some of the highest honours in Masonry, and at the time of his death was and had been for years the treasurer of his hospital lodge, by whose members he was regarded with deep affection.

He had a singularly happy family life, and rejoiced in the care and development of his country estate at Harpley. It was amusing to see him on his arrival in Worcestershire cast off the trappings of his profession and become the complete country squire—visiting his tenants, entertaining his guests, and reading the lessons in the village church. He had an eighteenth-century outlook on the importance of the family which was most refreshing in these days of changing values. By his numerous friends, so many of whom were outside his own profession, he will be remembered as a most kindly and lovable man, very ready to laugh, even at himself, and even more ready to help those in trouble. With his passing we lose still one more member of our profession nurtured in the traditions of a freer and easier past.

Dr. J. B. Gurney Smith writes: May I be allowed to pay tribute to a very revered teacher and chief in the unexpected passing of Dr. Geoffrey Evans? I feel that the whole profession in general, and Bart's in particular, have lost a very remarkable personality. No one could be in his company or listen to his words of erudition without feeling intensely stimulated. He radiated confidence and happiness. When I was a clerk in the firm, run as it then was by Lord Horder and himself, I could but feel I was drinking at the very fountain of authentic clinical medicine. He was possessed of a distinctly psychosomatic approach. When Lord Horder retired and Evans took over the firm as full physician and delivered clinical lectures he invariably chose topics of great relevance to clinical medicine. As a lecturer he was unsurpassed. I recall vividly the final words of Lord Horder's last clinical lecture at Bart's, when he said: "And now I take off my ward coat and hand it to you, Evans, my

friend. You and Gow have been loyal, inspiring, and charitable colleagues."

His fund of quips and stories, which he used with effect to brighten his ward rounds and lectures, was famous. Always distinguished in appearance, his attire seldom varied. As he always said, "If you always dress the same, your patient gets to know you." His laugh was wonderfully infectious. He was universally popular and beloved at Bart's, and his untimely death leaves a gap that will never be filled. In these days of nationalized medicine his wise utterances were needed more than ever, as he had a deep consciousness of the ethics of medicine, and—to borrow a phrase often on his lips—of "the structure and function of" our art. He was undoubtedly one of the most effulgent luminaries in the modern clinical firmament, whose brilliance was reflected in all his teaching. Another lovable and devoted son of Bart's has thus gone, but he has left us a wonderful example to follow.

F. W. M. L.-B. writes: To be a patient of Dr. Geoffrey Evans was a satisfying experience in time of necessity. At first meeting wonder might arise about what this man of slight physique and enigmatic expression had to give; but this was soon dispelled, and one was aware of the strength of an observant and integrated personality. In the street and in the corridors of hospitals and nursing-homes he moved with speed and decision; but in the quiet of his beautiful consulting-room and at the bedside he produced an effect of timelessness. He at once assumed command, while quietly listening to his patient, making rapid assessment of his or her need but seeking a common ground of interest which would allow of ease of communication and thus bring into being such intelligent co-operation as might be possible. The observant could not but be aware of the fine shape of his head, of the kindness of his guarded eyes, and of the sure touch of the firm hands which so swiftly played their part. His examination at an end, then was clearly spoken all the help he could give directly to the patient—often with humour, but without trace of facetiousness; always with that grave sensibility of the presence of the "Friend behind phenomena." In his untimely death a fine physician is lost to the profession he loved and served so well; and those who had the privilege of his friendship truly mourn his passing.

## Sir WALTER JOHNSON, C.M.G., M.B., F.R.C.S.

H.W.D. contributes the following note on Sir Walter Johnson, whose death was recorded in our issue of July 21 (p. 180): Of a somewhat retiring disposition and of simple tastes, Johnson did not seek wealth or publicity. His unspoken impelling motive was service for others. This accounted for his not publishing much on his professional achievements or as a traveller except for a few scientific papers on sleeping sickness, which he published with Lloyd and Rawson. His love of nature found expression in the beautiful gardens he made wherever he had his home, and he was never happier than when carrying out tsetse-fly research in the jungles and primeval forests, or travelling across deserts and among mountains and valleys in Africa, Europe, and America. Endowed with a wonderful physique, fearlessness, and tireless energy, he undertook some formidable and hazardous journeys in remote parts of Central and North Africa. Of these his most remarkable achievement was a journey in 1930 from Lagos to London in a Ford truck accompanied only by his sister, Miss Mary Johnson, M.B.E. The route was through Northern Nigeria, across the Sahara to Algiers and Tangier, shipment over the Mediterranean, and on through Spain and France to Calais. At that time present-day facilities in the Sahara for refuelling and repairs were negligible. They had to carry on their truck the supplies of petrol, water, spare parts, and food necessary for the long uncharted sand stretches between remote places where they might or might not refill. Other great journeys by truck in Africa were from Lagos to Cairo through the Belgian Congo, Uganda, Kenya, and the Sudan, returning to Lagos via Khartum, Lake Chad, and the Belgian Congo, and in 1936 from Lagos to Capetown.

During the six years at the Basutoland Leper Settlement he and his sister devoted their lives and much of their income to devising and creating interests and occupation for the patients. This work included classes for the manufacture of rugs from raw wool, holding cinema shows twice a week, and starting Boy Scout and Girl Guide companies—all of which contributed to the success of other therapeutic measures. He was unmarried, and for the greater part of his service in Nigeria and during the latter fourteen years of his life in South Africa his sister shared his home, where their cordial hospitality and friendship will long be remembered by their many privileged friends.

## CHARLES E. S. FLEMMING, M.R.C.S.

Dr. Charles Flemming, whose death on August 26 we regret to announce, was as excellent an example of the country doctor as could be found in rural England. He spent his whole life on one short stretch of countryside on the borders of Somerset and Wiltshire. His birthplace, his medical school, the scene of his practice for half a century or more, and the retreat of his old age were distant from one another by only a few miles. With abilities far above the ordinary and a personality that made itself felt in any company, he was content to live among and serve the people with whom he had been brought up, as his father had been before him. Probably he thought no vocation more worthy of the best that a man could give. His own nature seemed to partake of the kindliness of the country in which he lived. He never lost a certain boyish smile and country freshness, and even when he spoke in medico-political meetings or discussed policy in committees one felt that his heart was in his garden, which was his only hobby.

Charles Edward Stewart Flemming was born on May 10, 1863, at Freshford in Somerset, the little village where the Frome meets the Avon five miles below Bath. In the parish church of Freshford there is a memorial window to his father, T. H. Flemming, M.D., erected in 1895. He was educated at Somerset College, Bath, and took his medical training at Bristol Medical School, qualifying in 1886, and joining the British Medical Association in the same year. After holding a resident post at Winsley Sanatorium in his own neighbourhood, he settled down in practice in the picturesque little town of Bradford-on-Avon, with its stone-built gable-fronted houses, eventually becoming the head of a medical firm of four partners. For a quarter of a century Flemming was an insurance practitioner on the county panels of Somerset and Wiltshire, and he rejoiced in the opportunities of a country doctor to know his patients and their lives in a way only rarely possible to his colleague in the

town. His long years in practice in one locality enabled him to study the changes in incidence and character of disease as affecting a particular community over two generations, and in 1926, in an interesting paper to the Bath Clinical Society, he gave his impressions of the decline in frequency and in severity of attack of certain morbid conditions which he had noted during 40 years. First in the list of "disappearing diseases" in ordinary surgery and consulting-room practice he placed anaemia.

It can hardly be said when Flemming's work for the B.M.A. began. He took an active interest in its local organization for many years, and eventually became president of the Wiltshire Branch from 1922 to 1925. But by that time he was immersed in central affairs. As far back as 1903, when Mr. Andrew Clark was Chairman of the Association, and the Representative Body was just coming into existence, Flemming became a member of the Central Council, and with one or two short intervals he remained a member until 1939. He was a member also of every committee and subcommittee which had anything to do with medical politics, though his main interests were concerned with the medical examination and treatment of schoolchildren and with maternity and child welfare work. As a general practitioner he watched with a jealous eye the growth of the public health service, and, rather in opposition at one time to the policy of the Association, he strongly urged the appointment of general practitioners as part-time medical officers of health. In 1920 he was appointed by the Minister of Health a member of the Consultative Council on Medical and Allied Services and signed the Dawson report. Later he was also a member of the committee set up by the Minister to investigate the causes of maternal mortality.

Of the Hospitals Committee of the B.M.A. he was a member for twenty years and did much in his quiet way to shape the hospital policy of the Association. He believed strongly in what he called the "general practitioners' hospital," meaning by that term an auxiliary institution, but larger than the cottage hospital, where the local general practitioner might have in effect a nursing-home and be sure of a proper opportunity of using his powers of diagnosis and treatment. He thought it would be a good plan if local authorities could be influenced to appropriate some of their institutions for this purpose. He had in mind that large class of patients whose condition does not call for the highly specialized services of a large hospital but whom it is most unsatisfactory for the general practitioner to treat in their own homes.

He was vice-president of the Section of Medical Sociology at the Annual Meeting in Glasgow in 1922 and president of the same Section at the Bath Meeting in 1925. He had also represented the Association on the council of the Society of Medical Officers of Health. At one time he was a member of the Wiltshire County Council and later a co-opted member of its Maternity and Child Welfare Subcommittee.

Flemming made no pretensions to public oratory, but on the rare occasions when he spoke in debate he managed in his homely way to make his points. He suffered from a certain diffidence which perhaps hindered him from taking any high executive position in spite of his many years of service. He was, in any event, a man who preferred to be one of a team, and he did not aspire to any commanding position; but no man was regarded by his colleagues with greater affection.

## G. GREY TURNER, M.S., F.R.C.S.

Sir Allen Daley writes: I would like to pay tribute to my old friend, Professor George Grey Turner. He was invited by the University Selection Committee in 1934 to become the first professor of surgery at the British Postgraduate Medical School, and though it was a great financial sacrifice he accepted the offer. He played a prominent part in the development of the School, and consented to stay on after the normal retiring age until the end of the war made it possible to find a suitable successor. He was beloved by patients and staff. Always a glutton for work, he could go on indefinitely, provided he was fortified by frequent cups of tea. His presence at Hammersmith added enormously to the prestige of the School, and surgeons were attracted there from all over the world in order to profit by his long experience. Stories of "G. T." abound, and as the years go by they will be duly embellished and become part of the legendary history of the Postgraduate School. The world is much poorer by the passing of one who devoted his whole life to the welfare of his patients and the interests of medical education.

Dr. George Hurrell has sent us the following note to add to the obituary notices already published: Professor George Grey Turner was a member of "Sphalma," a small medical society or club that was founded in about the year 1900 in Newcastle-upon-Tyne, and which still holds regular meetings. The name "sphalma" comes from the Greek word meaning a fall or stumble, and the society was founded by the late Dr. Percival. Its membership was always limited to about twenty. It has held regular meetings during the winter months, usually following an evening meal. Before the first world war, when it was more active, the society had in addition one summer meeting in the form of a week-end excursion to either the Lake District or Scotland. The normal meetings were held in an informal friendly atmosphere, and no minutes or records were kept. A simple meal was followed by each member present, in turn, describing some mistake or error in diagnosis or treatment of a patient. Professor Grey Turner thoroughly enjoyed these meetings. The last one that he attended was on March 31, 1951, and at this meeting nine members were present.

"G. G.," as we always called him, was concerned about the declining membership of the society, because recently several of the older members had died. He made constructive suggestions about increasing the membership, and indeed he looked forward to further meetings in the autumn, when he hoped to meet several more of his old friends at an evening meal in the atmosphere of Sphalma. He himself thought that this little dining club was probably unique, and, as it had been in existence for about fifty years, he was very anxious that it should not die out. The official insignia of the society is an old silver snuff-box which belonged to a general practitioner member. A few years ago Professor Grey Turner presented a small ivory gavel with a little silver plate upon it for the use of the chairman at each meeting.

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Dr. MAX GREENBERG, whose death is reported from South Africa, was born in Lithuania in 1886. He went to South Africa with his family in 1889, when they settled in Kimberley. He always said that the fact that he took the part of a "medicine man" in a play at school when

he was 6 years old influenced his choice of a profession. He graduated M.B., Ch.B. from the University of Edinburgh in 1910, having graduated in the scheduled time, though he played as hard as he worked. He was interested in football, riding, dancing, skating, and particularly rowing, for which he received his rowing blue. After taking the F.R.C.S.Ed. in 1912 he returned to South Africa and took part in the 1914–18 war, seeing active service in South-west Africa. For a short while after being demobilized he acted as assistant to the late A. H. Watt, in Germiston, and then was appointed honorary surgeon at the Pretoria Hospital and railway surgeon in Pretoria. In 1923 he became consulting surgeon to the South African Railways in Johannesburg, and soon after was appointed honorary surgical registrar of the Johannesburg General Hospital. The "General" became one of his main interests, and he devoted a large part of his time to it, eventually becoming senior surgeon to the Transvaal Memorial Hospital for Children and serving on the hospital board for many years. He was Secretary of the Witwatersrand Branch of the B.M.A. for many years. In 1927 he was elected secretary of the Witwatersrand Branch of the Medical Association of South Africa, and was also responsible for a very successful medical congress held in Johannesburg. In addition, he served on the Federal Council. In 1935 he represented the Medical Association of South Africa at the Annual Representative Meeting in Britain and again in Australia. He was also elected representative of the Southern Transvaal Branch on the Johannesburg Hospital Board for three years. During the second world war he was not accepted for full-time military service, although he volunteered immediately war broke out, but did valuable work in a part-time capacity, with the rank of lieutenant-colonel, as surgeon for military patients at the General Hospital and in Pretoria. He gave his pay to charities. A connoisseur of the arts, Greenberg had one of the finest collections of paintings in South Africa, from which he gave several valuable examples of Africana to the City of Johannesburg in 1948 and 1950. On many occasions he assisted struggling artists financially, and one of his outstanding characteristics was his impulsive generosity. He was blunt and outspoken and by no means placid in temperament, but he never did a mean or underhand action, although his bluntness sometimes got him into difficulties. The Southern Transvaal Branch of the Medical Association of South Africa mourns the passing of Max Greenberg, one of its best-loved and keenest members.—R. B.

Dr. JAMES STEVENSON MORTON died in Boksburg, Transvaal, on July 21, aged 84 years. The elder son of Mr. James Morton, of Gilford, N. Ireland, he was born in 1867. He was educated at the Belfast Academy and then at Trinity College, Dublin, where he graduated in medicine in 1894, proceeding M.D. the next year. He studied midwifery at the Rotunda, and later took his D.P.H. at Cambridge. Dr. Morton went to South Africa in 1895, arriving in Boksburg on December 24 of that year. He was granted a licence to practise medicine in the Transvaal Republic under President Kruger. He joined the British Forces in 1899 at the outbreak of the Boer War, and was in Ladysmith throughout the historic siege. After the relief he was appointed to a hospital ship plying between South Africa and Britain, where he served until the armistice in 1902, when he returned to Boksburg. He was appointed M.O.H. for Boksburg in 1905 and served in that capacity until 1936. He did honorary work for the Boksburg-Benoni Hospital from the time of its opening until very recently, and, as well as carrying on general practice, was one of the East Rand Proprietary Mines doctors. Dr. Morton was a prominent member of the Masonic Lodge in Boksburg and took a keen interest in all public affairs. He continued in general practice until his last illness, in June this year, having been practising in Boksburg for 56 years. He leaves a widow and one daughter, his only son having been killed in action in the Royal Navy in 1945.

Mr. CHARLES MEADOWS-RYLEY, for 30 years ophthalmic surgeon to St. John's Hospital, Lewisham, met his death while bathing at Housel Cove, in his beloved Cornwall, on July 24, at the age of 65. From Emmanuel College, Cambridge, he went on to Guy's Hospital, and qualified M.R.C.S., L.R.C.P. in 1912. Three years later he graduated B.Chir, and in 1937 he took the Cambridge M.B. He held minor posts at Guy's Hospital, including that of assistant ophthalmic surgical registrar and tutor. In the 1914–18 war Meadows-Ryley was commissioned in the Royal Navy, and spent most of the time as ophthalmic surgeon to the Royal Naval Hospital, Chatham. He succeeded Sir Herbert Eason as ophthalmic surgeon to St. John's Hospital, Lewisham, 30 years ago, and his death occurred within one week of his official retirement from that post. He was also ophthalmic surgeon to Beckenham Hospital, and he had a very large consulting practice in the south-east of London. His writings were few, but he was an early and keen supporter of the Oxford Ophthalmological Congress. One of the technical advances with which he was associated was the introduction of diathermy in the treatment of eye diseases. He had many serious illnesses, including that bugbear of ophthalmic surgeons, glaucoma; this was successfully operated on by his old chief, Sir Herbert Eason, and he was able to carry on his work without any difficulty. A quiet, unassuming, upright man, Mr. Meadows-Ryley will be missed by his patients and by all his many friends.

Dr. A. D. SYMONS, medical officer of health for Shrewsbury, died at his home on August 28, aged 59. Arthur Denis Symons was born at Huddersfield in 1891, and received his early education at King Edward VI School, Bath, where his father was then headmaster. He entered Bristol University as a medical student in 1913, but volunteered for military service in August, 1914, and served with commissioned rank in the King's Royal Rifles for a period of two years, when he was recalled to complete his medical studies. After qualifying in 1918 he served six months in the Royal Navy as a temporary surgeon lieutenant. On his return from active service in three theatres of war he held the posts of house-surgeon and house-physician at the Bristol Royal Infirmary and resident medical officer at the Ham Green Isolation Hospital. In 1920 he took the D.P.H., and in the following year he proceeded to the degree of M.D. Coming to Shropshire as assistant county medical officer of health in 1922, he was appointed medical officer of health and school medical officer for the borough of Shrewsbury in 1925. During his undergraduate career he played cricket and rugby football for his university, and throughout his life he retained an active interest in these games. He was also a strong swimmer, and on two occasions—the last in 1930, when he rescued a 4-year-old boy by diving into the Severn—he was awarded the parchment of the Royal Humane Society. Symons took an active interest in the work of the B.M.A., and was elected president of the Shropshire and Mid-Wales Branch in 1949. As an after-dinner speaker, particularly at medical functions, he excelled, never failing to produce a timely jest and a word of wisdom. During his whole tenure of office as medical officer of health he succeeded admirably in combining excellent clinical work with high administrative ability; in fact he was as much at home at the bedside as in his office chair. He obtained an outlet for his considerable clinical acumen by his work for over 20 years as medical superintendent of Monkmoor Isolation Hospital, as well as at his regular school and infant-welfare clinics. His opinion on difficult cases of this type was frequently sought and greatly valued by practitioners in the area. He was among the first in the profession to appreciate the value of universal diphtheria immunization in infancy, and the scheme for immunization which he worked out for Shrewsbury proved most successful. During the second world war he was head of the civil defence casualty service for Shrewsbury. The welfare of all classes of the community and their progress towards a better, full, and more useful life were

matters that lay very close to his heart, and his forewords to his annual reports, written with clarity and elegance of style—as indeed befitted a nephew of the late A. E. Housman—were models of shrewd observation and careful thought for the future of his fellow citizens. Courageous in thought as in life, he maintained his interest in the future of medicine. Up to the last he remained a member of the planning committee and of the hospital management committee, and the full weight of his counsel was directed to the shaping of plans for better things to come. He is survived by his wife and three sons, to whom our sympathy is extended.—D. A. U.

# Medico-Legal

## BROKEN RIBS NOT DIAGNOSED

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

Damages amounting to £3,550 were awarded by Mr. Justice Pritchard in the High Court on May 24[1] in an action by Mrs. Margaret Kate Wood for negligence in respect of the death of her husband brought against a doctor and the board of governors of Charing Cross Hospital.

Mr. Wood, a manager of the accounts department of a bank, aged 49, spent the evening of August 6, 1948, out with two men friends. Between 7 p.m. and 9 p.m. they visited two public houses, and when walking west up the Strand at about 10 p.m. they came across a stationary lorry at the junction of the Strand with Bedford Street. Mr. Wood started to cross Bedford Street by crawling under the lorry just as the driver started to move off. One of its rear wheels pinned him to the ground, but did not go over him.

He lay on the pavement for a little while and then walked with his friends to the casualty department of Charing Cross Hospital just up the road, where he was seen by a doctor. The doctor's evidence was that Mr. Wood, who was intoxicated, repeatedly said that there was nothing the matter with him and that he wanted to go home. In examining him the doctor pressed his chest from front to back and from side to side and went over his skull for signs of injury, but found no clinical evidence of bone injury. Mr. Wood showed no signs of shock or pain, nor did the doctor find any crepitus, sweating, pallor, or abnormality. He did not use a stethoscope. Mr. Wood had told him what had happened.

After being treated for nose-bleeding Mr. Wood was sent home 11 miles in a taxi. In the early hours of the next day he was admitted to West Middlesex Hospital, where he died the same morning. At necropsy it was found that one collar bone and nine ribs on each side were fractured and his lungs were badly congested. One doctor gave the cause of death as shock, and another as leakage of air into the pleural cavity. Mr. Justice Pritchard held that Mr. Wood would probably not have died had he been immobilized at once.

In giving judgment Mr. Justice Pritchard said that Mr. Wood's intoxicated state should have put the doctor who examined him even more on his guard than usual rather than have deceived him as to his actual condition. The doctor had not exercised reasonable care in his examination. If a stethoscope had been used it was almost inevitable that Mr. Wood's true condition would have been discerned. The governors of the hospital, as his employers, were vicariously liable for the doctor's negligence. Mr. Justice Pritchard added that he hoped the doctor would not be daunted or unduly depressed and would find some consolation in the reflection that there were very few professional men who had not in their early stages made mistakes.

[1] *The Times*, May 25.

# Universities and Colleges

## UNIVERSITY OF OXFORD

In Congregation on July 28 the following medical degrees were conferred:

D.M.—W. H. Greany, B. S. B. Wood, *C. E. Davies.

M.CHIR.—R. H. Percival.

B.M.—P. Maton Terry, J. D. Granger, J. E. K. Moore, D. H. Taylor, J. D. Klauber, W. D. May, G. Rushworth, B. R. S. Mainwaring, Barbara M. Crumley, Leonora H. Goulty, Mary H. Miller, *B. M. Ogilvie, *J. A. P. Marston.

*In absence.

## UNIVERSITY OF CAMBRIDGE

Professor E. D. Adrian, O.M., P.R.S., has resigned from the Chair of Physiology, from September 30. Professor Adrian was recently appointed Master of Trinity College, Cambridge.

The trustees of the Nuffield Foundation have made a grant to the University of £7,000 for experiments in improved arrangements for medical care in East Anglia to be carried out under the direction of Professor A. Leslie Banks.

In Congregation on August 4 the following medical degrees were conferred:

M.D.—A. R. C. Butson, K. C. Robinson, J. Evans, W. T. C. Berry, E. H. Hare, J. McFie, M. B. McIlroy, D. P. Wheatley.

M.CHIR.—T. G. E. Loosemore.

M.B., B.CHIR.—R. H. Adrian, T. D. Anderson, W. D. Anderson, *P. T. Annesley, *R. S. Atkinson, *Margaret E. Barton, *R. J. Bennison, *M. Braimbridge, *E. J. F. Brewer, *J. S. N. Briggs, K. Brown-Grant, *W. M. Browne, *M. D. Cameron, *J. A. E. Clark, *P. B. Clark, *R. Cremona, *P. G. Cronk, N. L. Dallas, *J. J. Daly, *W. G. Davies, R. Dee, *J. H. Dickson, *W. Dorrell, *G. D. Downes, *D. C. Gibbs, *J. N. Gibson, J. R. Glover, *L. Golberg, *P. Goodall, L. R. H. Gracey, *D. M. Grant, Isobel H. Grant, J. H. Green, V. A. Grimshaw, *B. M. H. Hardman, *A. S. Harris, *Penelope A. Hewetson, *M. Hobsley, *C. A. Holborow, *R. G. Huntsman, *A. W. Johnston, *B. H. Kelham, J. C. Kelsey, *M. H. King, R. G. P. King, *Ivone Kinross, *T. P. Kissack, *Mrs. Rhoda R. Law, O. K. Litherland, *V. J. Marmery, Shelagh E. Marmion, *Mrs. Faith M. Mason, *I. H. Mills, K. H. G. Milne, *J. F. Moor, *G. H. Moss, *A. J. Palfrey, *R. H. Reynolds, *I. H. Robinson, *F. C. Rutter, *J. R. Savage, *J. R. Seale, *C. Shaldon, *D. W. Smith, *E. Stokoe, H. Sutherland, G. A. Taylor, *G. S. Thompson, *Rosemary F. Thompson, *Irene M. Watts, *Judith Weisz, *W. G. Wenley, I. H. Williams, *J. A. Williams, *R. T. Williams, *D. H. M. Woollam, G. H. Wright.

*By proxy.

## ROYAL COLLEGE OF SURGEONS OF EDINBURGH

At a meeting of the Royal College of Surgeons of Edinburgh held on July 25, with Mr. W. Quarry Wood, President, in the chair, the following candidates, having passed the requisite examinations, were admitted Fellows: J. S. Bains, R. A. Craven, S. W. Davidson, R. A. Denham, J. C. Grant, C. R. S. Jackson, D. A. Kernahan, Sylvia Lerer, M. P. Mehta, S. N. Peshin, H. D. Ritchie, K. Robertson, B. Sacks, S. J. Talsania, D. J. Toomey.

## CONJOINT BOARD IN SCOTLAND

The following candidates, having passed the final examinations, have been granted the diploma of L.R.C.P.Ed., L.R.C.S.Ed., L.R.F.P.S.Glas: M. A. Abdulla, A. I. Atta, W. M. Bezuidenhout, Cecily F. V. Borchards, E. G. Bredenkamp, G. W. Brown, D. W. Cameron, Sarah F. Charlton, Kim Choy Chong, J. Connelly, C. J. Constantinou, Flora M. Dale, Maureen F. Davies, R. E. Dean, J. T. F. de Graft-Johnson, Alice E. Fairbrother, G. I. Forbes, Rosemary M. J. Forsyth, H. W. Gardner, R. F. R. Gardner, F. B. C. Gouws, Joan T. Graham, W. M. Higginbottom, H. F. Jackson, Natalie M. Johnston, P. L. Kapur, B. S. Khehar, P. W. Lang, Elizabeth S. Latham, O. P. Le Breuilly, Margaret C. Lee, W. K. Lutterodt, I. I. M. MacGregor, D. T. Mackay, P. W. McLuskey, W. McPheat, J. R. MacPherson, J. H. Mendes, Violet V. M. Moody, J. A. Morny, Doreen A. Murray, K. L. Naidoo, Jeanie MacP. Orr, W. L. Parker, N. Rifkind, W. D. Roberts, Elizabeth M. Robertson, Wendy Scott, M. P. Shannon, D. L. P. Singh, H. B. Singh, F. Slane, Janet U. A. Smith, M. Snell, S. O. Too-Kong, Ellen M. Tulley, P. S. Vaithilingam, Vera M. Vodden, A. A. Volodarsky, E. K. B. Wells, Eirlys J. Williams, Sheila A. Yhap.

# INFECTIOUS DISEASES AND VITAL STATISTICS

We print below a summary of Infectious Diseases and Vital Statistics in the British Isles for the week ending August 18 (No. 33).

Figures of notified *cases* are for: (*a*) England and Wales (London included). (*b*) London (administrative county). (*c*) Scotland. (*d*) Northern Ireland. (*e*) Eire. Figures of *births and deaths* and of *deaths* recorded under each disease are for: (*a*) The 126 great towns in England and Wales (London included). (*b*) London (administrative county). (*c*) The 16 principal towns in Scotland. (*d*) The 10 principal towns in Northern Ireland. (*e*) The 13 principal towns in Eire. A dash — denotes no cases; a blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, Northern Ireland, and Eire, the Ministry of Health and Local Government of Northern Ireland, and the Department of Health of Eire.

| Disease | 1951 Week Ending August 18 | | | | | 1950 Corresponding Week | | | | | 1942–50 England & Wales Corresponding Week | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | (*a*) | (*b*) | (*c*) | (*d*) | (*e*) | (*a*) | (*b*) | (*c*) | (*d*) | (*e*) | Highest | Median | Lowest |
| Diphtheria | 31 | 3 | 8 | 1 | — | 31 | — | 15 | 4 | 1 | 626 | 251 | 31 |
| Deaths | — | — | — | | — | — | — | — | — | — | | | |
| Dysentery | 153 | 37 | 68 | 1 | | 141 | 13 | 99 | — | 2 | 259 | 141 | 35 |
| Deaths | | — | | | | | — | | — | | | | |
| Encephalitis, acute | 9 | — | — | — | | 13 | 1 | — | — | 1 | 13 | 3 | 1 |
| Deaths | | — | | | — | | — | | | — | | | |
| Erysipelas | | | 16 | 1 | 2 | | | 14 | 2 | 6 | | | |
| Food-poisoning | 118 | 18 | | 3 | | 160 | 19 | | 9 | | | | |
| Infective enteritis or diarrhoea under 2 years | | | | 22 | 52 | | | | 11 | | | | |
| Deaths | 11 | | 1 | | 1 | 10 | | 4 | 1 | 4 | | | |
| Measles* | 3,252 | 58 | 62 | 126 | 107 | 5,529 | 362 | 79 | 22 | 85 | 5,529 | 2,712 | 1,069 |
| Deaths | | — | — | | 1 | | | — | — | — | | | |
| Meningococcal infection | 25 | 2 | 12 | — | | 21 | 2 | 33 | 3 | 2 | 63 | 37 | 21 |
| Deaths | | — | — | | | | — | — | | | | | |
| Ophthalmia neonatorum | 34 | 1 | 10 | — | 1 | 35 | 9 | 11 | — | | 90 | 58 | 35 |
| Pneumonia, influenzal | 233 | 7 | 4 | 3 | | 233 | 8 | 1 | 2 | | 347 | 275 | 233 |
| Deaths (from influenza)† | 3 | — | — | | 1 | 3 | — | — | — | 1 | | | |
| Pneumonia, primary | | | 80 | | | | | 98 | | | | | |
| Deaths | 119 | 16 | | | 3 | 76 | 9 | | 9 | 2 | | | |
| Poliomyelitis, acute: | | | | | | | | | | | | | |
| Paralytic | 57 | 3 | 14 | 3 | | 550 | 38 | 65 | 18 | 8 | 691 | 34 | 15 |
| Non-paralytic | 63 | 5 | | | | | | | | | | | |
| Deaths§ | 5 | — | | | — | 26 | 2 | | | 1 | | | |
| Puerperal fever | | | 8 | | 1 | | — | 3 | | | | | |
| Puerperal pyrexia‖ | 249 | 29 | 9 | | 1 | 80 | 8 | 7 | — | 1 | 172 | 127 | 80 |
| Scarlet fever | 477 | 47 | 92 | 12 | 17 | 614 | 26 | 94 | 39 | 36 | 1,525 | 736 | 614 |
| Deaths | | — | — | | — | | | — | — | — | | | |
| Smallpox | — | — | — | — | | — | — | — | — | | | | |
| Deaths | | | | | | | | | — | | | | |
| (1) Tuberculosis, respiratory | | | 114 | 28 | | | | 116 | 37 | | | | |
| (2) Tuberculosis, non-respiratory | | | 24 | 12 | | | | 29 | 4 | | | | |
| (1) Deaths | 104 | 14 | 22 | | 5 | 138 | 14 | 27 | 4 | 12 | | | |
| (2) Deaths | | — | 6 | | 4 | | 7 | 5 | — | 3 | | | |
| Typhoid fever | 10 | — | — | 1 | 1 | 9 | — | — | — | 1 | | | |
| Deaths ¶ | — | — | — | | | — | — | — | — | | | | |
| Paratyphoid fever | 52 | 2 | 5 (B) | 3 | 2 (B) | 9 | — | 1 (B) | — | | 113 | 22 | 9 |
| Whooping-cough | 3,159 | 154 | 273 | 55 | 60 | 3,939 | 336 | 220 | 33 | 61 | 3,939 | 1,870 | 967 |
| Deaths | 2 | — | — | | 1 | 1 | 1 | — | — | 1 | | | |
| Deaths (0–1 year) | 192 | 23 | 26 | | 12 | 196 | 23 | 17 | 6 | 20 | 329 | 300 | 196 |
| Deaths (excluding stillbirths) | 3,918 | 592 | 487 | | 135 | 3,886 | 577 | 481 | 101 | 166 | 3,910 | 3,765 | 3,618 |
| Annual death rate (per 1,000 persons living) | | | 10·0 | | | | | 9·7 | | | | | |
| Live births | 6,921 | 1,093 | 833 | | 490 | 7,061 | 1,150 | 821 | 209 | 323 | 9,005 | 7,060 | 5,749 |
| Annual rate per 1,000 persons living | | | 17·1 | | | | | 16·5 | | | | | |
| Stillbirths | 177 | 15 | 27 | | | 179 | 15 | 20 | | | 274 | 201 | 175 |
| Rate per 1,000 total births (including stillborn) | | | 31 | | | | | 24 | | | | | |

* Measles not notifiable in Scotland and returns are approximate. † Includes primary form for England and Wales, London, and N. Ireland. § The number of deaths from poliomyelitis and polio-encephalitis for England and Wales, and London (administrative county), are combined. ‖ Includes puerperal fever for England and Wales and for Eire. ¶ Deaths from paratyphoid fever are combined with those from typhoid fever. Figures for births and deaths for Northern Ireland have not yet been received.

# Vital Statistics

### Salmonella in Tortoises

Investigations have shown that a large number of tortoises recently imported into this country harbour salmonella organisms. Salmonellae have been found in all the tortoises investigated with the possible exception of one of them, but the salmonellae did not include any of the common human pathogens. In particular, *Salmonella paratyphi-B* has not been found. A tortoise was suspected of having infected a child with *Salmonella paratyphi-B*, but repeated examinations of the tortoise failed to discover this organism in it. No case of human infection has been traced to a tortoise. All the tortoises examined have come from Africa, and include a large batch from Casablanca; none are from the American continent.

### Puerperal Pyrexia Notifications

The change in the definition of notifiable puerperal pyrexia introduced on August 1 in England and Wales has greatly increased the number of notifications sent weekly to the General Register Office. In the first 28 weeks of this year the average weekly number of notifications was 80: the lowest number was 53 in the twenty-sixth week, and the highest number was 106 in the third week. Reference to the Graph in the next column shows how great has been the increase in notifications recently.

In the last week before the new definition came in the number of notifications was 114—higher than any previous number this year—but this seems to have been merely a chance variation. The effect of the new definition is shown in the Table below, with alongside the figures for puerperal fever and puerperal pyrexia in Scotland, where the new definition has not been introduced.

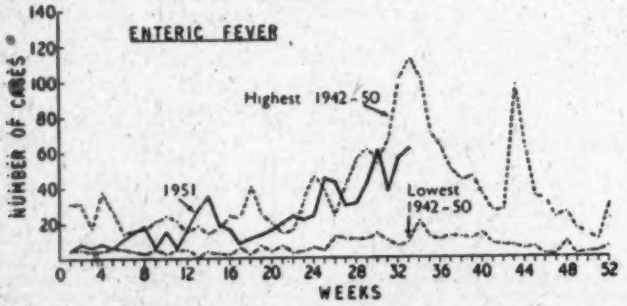
*Notifications of Puerperal Pyrexia and Puerperal Fever*

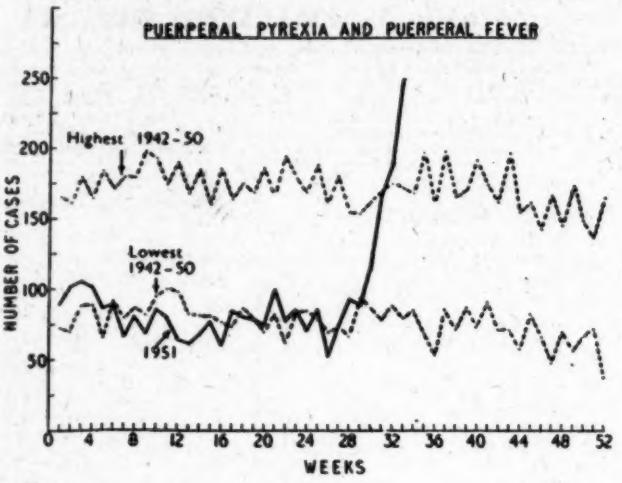
| Week Ending | England and Wales | Scotland |
|---|---|---|
| July 21 .. .. .. | 89 | 18 |
| July 28 .. .. .. | 114 | 14 |
| Aug. 4 .. .. .. | 167 | 9 |
| Aug. 11 .. .. .. | 189 | 17 |
| Aug. 18 .. .. .. | 249 | 17 |
| Aug. 25 .. .. .. | 240 | 8 |

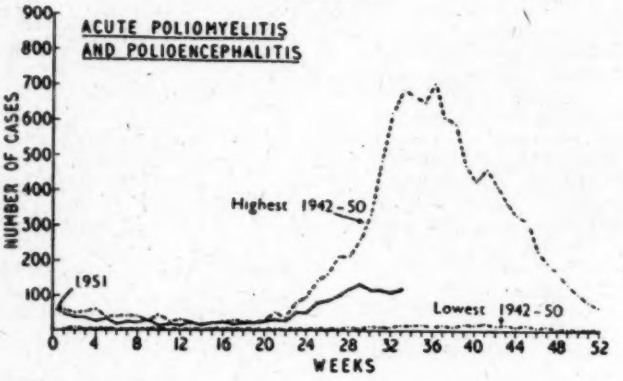
Under the new definition puerperal pyrexia becomes notifiable when a temperature of 100.4° F. (38° C.) or more occurs within 14 days after childbirth or miscarriage. Previously, though the time was longer (21 days) within which the temperature had to rise to 100.4° F. to become notifiable, the temperature had either to be sustained during a period of 24 hours or to have recurred during that period.

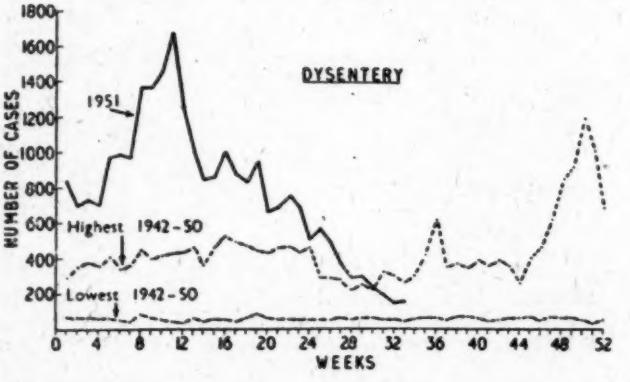
### Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported during the nine years 1942–50 are shown thus - - - - - - -, the figures for 1951 thus ————. Except for the curves showing notifications in 1951, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.




### Infectious Diseases

The only variations of any size in the number of notifications during the week ending August 18 in England and Wales were an increase of 498 for whooping-cough and a decrease of 369 for measles.

A small rise in the incidence of whooping-cough was recorded in most regions of the country; the largest rises were Yorkshire West Riding 93, Lancashire 78, and Surrey 49. For the twelfth consecutive week a fall was recorded in the number of notifications of measles; the largest decline during the week was 128 in Kent. The notifications of scarlet fever were 9 more than in the preceding week; no fluctuations of any size were recorded in the local trends. After reaching a record low level in the preceding week a rise of 12 in the number of notifications of diphtheria caused the incidence to revert to its previous level. An increase of 3 in the number of notifications of diphtheria was reported from London, Lancashire, Staffordshire, and Yorkshire West Riding.

The relatively high level of paratyphoid fever was maintained, 9 of the 52 cases being notified in Birmingham C.B.

The number of notifications of dysentery was 4 more than in the preceding week. The largest returns were:

London 37 (Islington 13), Kent 26 (Malling R.D. 24), Lancashire 16.

A small rise occurred in the incidence of acute poliomyelitis, and the paralytic cases were 2 more and the non-paralytic cases 6 more than in the preceding week. The largest returns during the week were: Lancashire 15, Yorkshire West Riding 13, Kent 10, and London 8.

### Poliomyelitis

Poliomyelitis notifications in the week ending August 25 were as follows (figures for the previous week in parentheses): paralytic, 60 (57); non-paralytic, 56 (63); total, 116 (120). Up to and including the week ending August 25 the overall notification rate for England and Wales was 3.99 per 100,000.

Although the proportion of non-paralytic cases tends to fall compared with the previous weeks, it was still 48% for the week under review, which is higher than the normal. Some districts which have notified 15 or more cases in the year to date (with incidence per 100,000 in parentheses) are as follows: Coventry C.B., 89 (34.71); Orpington U.D., 56 (94.64); Swansea C.B., 24 (14.88); Rotherham R.D., 20 (42.60); Woolwich M.B., 16 (11.2); Northampton C.B., 16 (15.36).

### Industrial Accidents and Diseases

The number of workpeople (other than seamen) in the United Kingdom whose deaths from accidents in the course of their employment were reported in July was 142, compared with 104 (revised figure) in the previous month and 120 (revised figure) in July, 1950 (*Ministry of Labour Gazette*, August, 1951). Of these deaths 36 were underground in coal mines.

There were 5 cases of lead poisoning (smelting of metals 3), 5 cases of anthrax, 10 of epitheliomatous ulceration, and 19 of chrome ulceration (chromium plating 16). There was 1 death due to toxic anaemia.

During the 13 weeks ending June 30, 1951, the number of people killed in coal-mine accidents in Great Britain was 162, compared with 124 in the 13 weeks ending March 31, and 97 (revised figure) in the 13 weeks ending July 1, 1950. Of these 162 deaths, 83 occurred in the disaster at Easington Colliery, Durham, on May 29, 1951.

### Week Ending August 25

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 463, whooping-cough 2,948, diphtheria 23, measles 2,352, acute pneumonia 181, acute poliomyelitis 116, dysentery 174, paratyphoid fever 46, and typhoid fever 6.

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The *Medico-Legal Journal* is published quarterly, and at the end of each issue abstracts of papers are printed. One of these (Part II, 1951, p. 73) deals with medicine in the tenth century in Wales. Doctors were officers of the royal courts and were ranked last but one in order of precedence. They were paid a fixed salary and treated members of the court for nothing; the only exceptions to the rule were the special fees paid by patients with any of the three "dangerous wounds"—wounds of the head or abdomen, or fractured limbs. Welsh law placed a fixed value on honour, men and women's limbs, cattle, and other property. The doctor's worth according to rank was 126 head of cattle, and the fine payable if he were insulted was six head of cattle and six score of silver. Compensation for injuries to the body was paid according to a single scale, regardless of rank, and for assessment the body was divided into 14 parts, the tongue being the principal member because "it defended the rest." The thumb and the big toe were valued at double the fingers and toes; teeth were 2s. each, blood also 2s., and every bone of any size was considered worth 20d.

# Medical News

### Emergency Bed Service: Applications and Admissions

During the seven days ending September 3 the number of applications made by doctors to the London Emergency Bed Service for admission of patients was 668, of which 93.4% were admitted. This information will in future be published weekly in these columns. The applications include those from general practitioners and those from hospitals wanting to transfer patients from their casualty or out-patient departments. The gap between the number of applications and the number admitted is not composed entirely of cases that fail to be admitted. Some are cases withdrawn by the doctor or hospital while the E.B.S. is still working on the case, and some cases are of patients who refuse to go to hospital when a bed has been found or who die before admission.

### International Meeting of Voluntary Anti-tuberculosis Organizations

For the first time secretaries of national anti-tuberculosis associations—the majority of them independent voluntary bodies—will meet in committee in Paris on September 10 and 11, in connexion with the council meeting of the International Union Against Tuberculosis, to discuss the social and educational side of the control of tuberculosis. National associations from no fewer than 50 countries are concerned, and the discussion will cover the organization of national anti-tuberculosis bodies and social legislation connected with tuberculosis (Dr. Gedde-Dahl, Norway); methods of raising funds for anti-tuberculosis work (a French speaker); training and opportunities for non-medical men and women engaged in the anti-tuberculosis campaign (Dr. James E. Perkins, U.S.A.); and methods and problems of health education (Dr. J. Kroondijk, Holland). One of the main features in the handling of tuberculosis in Great Britain is the strong part which voluntary and non-official organizations play even to-day with the National Health Service financed by the Government. These bodies not only look after individual tuberculous patients in ways which the official schemes do not cover, but represent a mighty force of public opinion. Throughout the British Commonwealth—in India, Australia, Canada, South Africa, and New Zealand, as well as in many British Colonies—there are similar voluntary agencies keeping Governments up to the work.

### Forensic Pathology

The British Association of Forensic Pathologists, which was founded a year ago under the presidency of Sir Sydney Smith, held its second meeting in Edinburgh on June 16. Papers were read on "Assisted Asphyxia in the Newborn" (Dr. Keith Simpson), "Chronic Mercury Poisoning in Latent Fingerprint Development" (Dr. Gilbert Forbes), "Group Specific Substances in Sweat Stains" (Dr. F. S. Fiddes), "A Recent Case of Exhumation" (Dr. D. E. Price), "A Possible Case of Sensitivity to 'Anthisan'" (Dr. Donald Teare), and a paper on the identification of some skeletal remains (Dr. J. Imrie). The papers were accompanied by a critical and lively discussion. A third meeting is planned for November 24 at Guy's Hospital: in the morning there will be an open discussion on "The Interpretation of Asphyxial Signs" and "Separate Existence"; in the afternoon the society will meet in private to discuss cases of special pathologico-forensic interest. Fellowship and membership of the new society are limited to doctors engaged principally in the practice and teaching of forensic medicine, but associate membership is open to any doctor who is interested in the subject. The secretary of the society is Dr. F. E. Camps, 79, Harley Street, W.1, to whom those wishing for further information should apply.

### Essay Award

The American College of Chest Physicians offers a cash prize award of $250 to be given annually for the best original contribution, preferably by a young investigator, on any phase relating to chest disease. The prize is open to contestants from all countries. The winning contribution will be selected by a board of judges, and the award, together with a certificate of merit, will be made at the forthcoming annual meeting of the College. Second- and third-prize certificates will also be awarded. All manuscripts submitted become the property of the American College of Chest Physicians and will be referred to the editorial board of the college journal, *Diseases of the Chest*, for consideration. Contestants are advised to study the format of the journal as to length, form, and arrangement of illustrations, to guide them in the preparation of the manuscript. These conditions must be observed: (1) Five copies of the manuscript, typewritten in English, should be submitted to the executive office, American College of Chest Physicians, 112, East Chestnut Street, Chicago 11, Illinois, not later than April 1, 1952. (2) The only means of identification of the author or authors shall be a motto or other device on the title page, and a sealed envelope bearing the same motto on the outside, enclosing the name of the author or authors.

### R.M.P.A. Prize Award

The Burlingame Prize (value £100) of the Royal Medico-Psychological Association has been awarded to Dr. Martin Roth, director of clinical research, Graylingwell Hospital, Chichester, for his paper on "Changes in the E.E.G. under Barbiturate Anaesthesia Produced by Electro-convulsive Treatment and Their Significance for the Theory of E.C.T. Action."

### West London Medico-Chirurgical Society

The Triennial Gold Medal of the Society has been awarded to Dr. C. H. Slocumb, of the Mayo Clinic, for his work on cortisone and A.C.T.H., and will be presented to him by the president, Mr. B. Sangster Simmonds, at a dinner-meeting to be held at South Kensington Hotel, 41, Queen's Gate Terrace, London, S.W., on Friday, October 5, 1951.

### Medical Research Council Travelling Awards

The Medical Research Council announces that travelling awards in ophthalmology and otology under the Alexander Pigott Wernher Memorial Trust, tenable during the academic year 1951–2, have been made to Dr. Patricia R. Davey (Sydney, Australia) and Dr. R. N. Misra (Medical College, Lucknow, India).

### Wills

Mr. George Edward Pearson left £148,117. He left £1,000 to the Benevolent Fund of the Pharmaceutical Society of Great Britain, and after other bequests the residue equally between St. Dunstan's, the Church of England Children's Society, King George's Fund for Sailors, and King Edward's Hospital Fund for London. Dr. Horace Middleton Vernon left £12,542. He left £300 to the council of the National Institute of Industrial Psychology, conditional upon its being used to found a prize, to be awarded every second year, to the investigator who, being a British subject and being under the age of 45 years, has in the opinion of the council done the most valuable research work in the subject of industrial psychology and physiology. Mr. Robert Moran Galloway left £37,898: after the death of the beneficiaries certain trust funds were to be shared between the British Legion Officers Benevolent Department, the National Institution for the Blind, the National Institution for the Deaf, London Lock Hospital and Home, the R.A.F. Benevolent Fund, the Royal U.K. Beneficent Association, the Ivory Cross Dental Hospital, and the North Devon Infirmary, Barnstaple.

## COMING EVENTS

### International Meeting of Neuropathologists

An announcement of the first international meeting of neuropathologists was published in the *Journal* of August 25 (p. 504). We are now informed that the meeting will be held at Rome from September 8 to 13, 1952.

### Westminster Medical School

The inaugural address at the opening of the 1951–2 session of Westminster Medical School will be given by the Very Rev. John Lowe, vice-chancellor of the University of Oxford, at Church House, Great Smith Street, London, S.W., on Monday, October 1, at 3 p.m.

### Institute of Dermatology

The winter course of lectures at the institute (St. John's Hospital for Diseases of the Skin, Lisle Street, Leicester Square, London, W.C.) begins on October 2. The syllabus has been considerably expanded this year, and lecturers have been invited to deal with subjects allied to dermatology. The pattern of the course is that systematic lectures will be given on Tuesdays, and clinical demonstrations on Fridays pertinent to the subject of the lecture on the previous Tuesday as far as possible. Lectures and demonstrations on pathology, including medical mycology, will be given on Wednesdays and Thursdays, and lectures on *x*-ray technique will be included on certain Wednesdays.

### Institute of Urology

A series of postgraduate lectures, arranged by the Institute of Urology in association with St. Peter's and St. Paul's Hospitals, will be given at St. Paul's Hospital, Endell Street, London, W.C., on Wednesdays, at 4.30 for 5 p.m., from October 3 to December 19, 1951, both dates inclusive.

### Course in Physical Medicine

It is proposed to hold a course for Part II of the diploma on Saturday mornings during October, November, December, and January. Demonstrations will be held at the following hospitals: King's College Hospital, London Hospital, Middlesex Hospital, University College Hospital. In addition there will be demonstrations in orthopaedics and neurology. The fee for the course will be two guineas. Those intending to take part should apply to the honorary secretary, British Association of Physical Medicine, 45, Lincoln's Inn Fields, London, W.C.2, by September 15, 1951.

### Churches' Council of Healing

A course of six lectures on "Divine Healing in Everyday Action" will be given at the Alliance Hall, Palmer Street, Westminster, London, S.W., on September 28, October 19, November 16, December 10, 1951, January 18 and February 29, 1952, at 7 p.m. The last lecture will be given by Dr. E. E. Claxton on "The Vision of the Future." Full particulars may be obtained from the secretary of the council, Swallowfield Lodge, Keymer, Hassocks, Sussex.

## SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

#### Monday

CHURCH OF ENGLAND HOSPITAL CHAPLAINS' FELLOWSHIP.—At Royal Free Hospital School of Medicine, 8, Hunter Street, London, W.C., September 10, 2.30 p.m. Meeting.

#### Tuesday

EDINBURGH POSTGRADUATE BOARD FOR MEDICINE.—At Edinburgh University (Anatomy Lecture Theatre), September 11, 4.30 p.m., "*Internal Hydrocephalus*," by Professor Dorothy S. Russell.

## APPOINTMENTS

EAST ANGLIAN REGIONAL HOSPITAL BOARD.—*Part-time Consultant Obstetrician and Gynaecologist, Newmarket General Hospital*, J. S. Heaketh, M.B., B.Chir., M.R.C.O.G. *Part-time Consultant Physician, North Cambridgeshire Hospital, Wisbech, and Doddington Hospital*, F. G. Pattrick, M.B., B.Chir., M.R.C.P.Ed., D.T.M.&H. *Consultant Orthopaedic Surgeon in Peterborough and King's Lynn Area*, A. B. King, M.B., B.S., F.R.C.S. *Assistant Psychiatrist, Hellesdon Mental Hospital*, J. V. Fennell, M.B., B.Ch., D.P.M. *Assistant Psychiatrist, Fulbourn Mental Hospital*, G. J. F. Fryer, M.R.C.S., L.R.C.P., D.P.M. *Surgical Registrar, East Suffolk and Ipswich Hospital and Ipswich Borough General Hospital*, H. F. McG. Bassett, M.B., B.S. *Medical Registrar, Papworth Sanatorium*, C. P. Silver, B.M., B.Ch., M.R.C.P. *Medical Registrar at East Suffolk and Ipswich Hospital and Ipswich Borough General Hospital*, K. T. Evans, M.B., Ch.B.

NORTH-EAST METROPOLITAN REGIONAL HOSPITAL BOARD.—*Part-time Consultant Surgeon, King George Hospital, Ilford*, C. P. Allen, M.B., Ch.B., F.R.C.S.Ed. *Part-time Consultant Psychiatrist, Ilford Child Guidance Clinic*, Winifred M. Burbury, M.B., B.S., D.P.M. *Part-time Consultant Anaesthetists*, Dorothea B. I. Halstead, M.B., Ch.B., D.A., D.C.H. (at St. George-in-the-East Hospital), G. Herington, M.B., B.S., D.A. (at Tilbury and Riverside Hospital), B. Kenton, M.R.C.S., L.R.C.P., D.A., D.C.H. (at Bethnal Green Hospital), B. P. Armstrong, M.R.C.S., L.R.C.P., D.A. (at Mildmay Mission Hospital). *Part-time Consultant Obstetricians and Gynaecologists*, Joan E. M. Lambert, M.R.C.S., L.R.C.P., M.R.C.O.G., and D. J. MacRae, M.D., F.R.C.S.Ed., M.R.C.O.G. (at the Mothers' (Salvation Army) Hospital), I. Bierer, M.D. (at Bethnal Green Hospital).

THORBURN, A. LENNOX, M.D., D.P.H., Tuberculosis Physician, Manchester Regional Hospital Board.

THORNE, NAPIER A., M.D., M.R.C.P., Senior Registrar to Skin Department, London Hospital, E.

WATKIN, IESTYN MORGAN, Ph.D., M.Sc., M.B., B.Ch., D.P.H., Medical Officer of Health, Combined District Councils of Cardiganshire and Assistant County Medical Officer of Health.

## BIRTHS, MARRIAGES, AND DEATHS

### BIRTHS

**Anderson.**—On August 21, 1951, at Windsor, to Audrey (formerly Northcott), wife of Dr. J. L. Anderson, a son—Timothy James.

**Blair.**—On August 25, 1951, at Inverness, to Lois (formerly Gilbert), M.B., Ch.B., wife of Robert A. Blair, M.B., Ch.B., F.R.F.P.S.Glas., a son.

**Graves.**—On August 22, 1951, at "Sunnyside," Writtle, Essex, to Valerie (formerly Scotland), M.B., B.S., wife of J. C. Graves, M.R.C.S., L.R.C.P., a son.

**Holden.**—On August 26, 1951, at Singapore, to Dr. Ursula Holden (formerly Stanley), wife of Surgeon Lieutenant P. H. Holden, R.N., a daughter.

**Moodie.**—On August 28, 1951, at Dundee, to Barbara (formerly Jeffery), M.B., B.S., wife of Gordon Moodie, M.B., B.S., a daughter—Helen Elizabeth.

**Scriven.**—On August 30, 1951, at Gally Hill Nursing Home, Church Crookham, Hants, to Dr Jeanne Scriven (formerly Edwards), wife of Dr. W. H. Scriven, M.B.E., a son.

**Stewart.**—On August 15, 1951, at Romford, to Evalyn (formerly Linscott), wife of Dr. J. M. Stewart, D.M.R.D., a son.

**Thompson.**—On August 28, 1951, to Joan (formerly Murray), wife of Blair A. Thompson, F.R.C.S.Ed., a daughter.

### DEATHS

**Bowie.**—On August 20, 1951, at Poyle Place, Colnbrook, Bucks, Alexander Bowie, M.D., aged 92.

**Butterworth.**—On August 18, 1951, at his home, Stanton House, Rhos-on-Sea, Colwyn Bay, Charles Edward Butterworth, M.B., Ch.B.

**Cardinall.**—On August 17, 1951, at Triangle House, Hatfield, Herts, Charles Daking Cardinall, M.R.C.S., L.R.C.P., aged 82.

**Exmouth.**—On August 19, 1951, at Bovey Tracey, Devon, Edward Irving Pownoll Pellew, O.B.E., M.R.C.S., L.R.C.P., Viscount Exmouth, aged 84.

**Goodwin.**—On July 8, 1951, at Vancouver, British Columbia, Guy Stewart Goodwin, M.D.

**Green.**—On August 22, 1951, at Little Brandon, Portsdown Hill Road, Cosham, Hants, Philip Halbert Green, M.B., Ch.B., aged 73.

**Grellet.**—On August 22, 1951, William Pennington Grellet, L.R.C.P.&S.Ed., L.R.F.P.S., aged 76.

**Harrison.**—On August 15, 1951, at Godmanchester, Huntingdon, Newcome Herbert Harrison, M.R.C.S., L.R.C.P., L.D.S. R.C.S.

**Jubb.**—On August 14, 1951, at Scratby, Ormesby St. Margaret, Norfolk, Archibald Armitage Jubb, D.Sc., M.D., Brevet Major, R.A.M.C., retired, aged 76.

**Lambe.**—On August 19, 1951, at Findon, Sussex, Thomas Lambe, M.R.C.S., L.R.C.P., aged 81.

**Lavertine.**—On August 3, 1951, at Milestone Cottage, Havant, Hants, Albert Xavier Lavertine, L.R.C.P.&S.I., Surgeon Captain R.N., retired, aged 79.

**Marsh.**—On August 20, 1951, at 23, The Broadway, Thorpe Bay, Essex, Cecil John Marsh, L.S.A.

**Morton.**—On July 21, 1951, at Boksburg, Transvaal, South Africa, James Stevenson Morton, M.D., D.P.H., aged 84.

**Parker.**—On August 22, 1951, at 235, High Road, Harrow Weald, Middlesex, Athel Mary Parker (formerly Sayce), M.B., B.Ch., aged 46.

**Parry.**—On August 13, 1951, at 5, Carshalton Road, Blackpool, Thomas Wilfred Parry, M.B., Ch.B.

**Robertson.**—On August 7, 1951, Granville Douglas Robertson, F.R.C.S., of Robin Hill, Itchen Abbas, near Winchester, Hants.

**Scott.**—On August 3, 1951, Douglas Hay Scott, M.B., Ch.B., of 3, Corkran Road, Surbiton, Surrey.

**Smith.**—On August 2, 1951, at Leicester, Gayton Warwick Smith, M.D., D.P.H.

**Terry.**—On August 7, 1951, at 39, Raynes Road, Lee-on-Solent, Hants, Paul McKenna Terry, T.D., J.P., L.R.C.P.&S.Ed., aged 88.

**Thompson.**—On August 24, 1951, at Harrogate, Arthur Hirst Thompson, M.R.C.S., L.R.C.P., of "Carmires," Knaresborough, Yorks, aged 96.

**Walker.**—On August 5, 1951, at a Torquay nursing-home, Thomas Malcolm Walker, M.R.C.S., L.R.C.P., late R.A.M.C. and R.A.F.M.S., previously of Hook Norton, Oxon, and Hailsham, Sussex, aged 78.

# Any Questions?

*Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.*

### Why Isolate Scarlet Fever?

**Q.**—*Why is it that stress is laid on the isolation of scarlet fever and its notification, when the organism responsible is usually the same as in ordinary cases of tonsillitis? Surely the difference is only in the erythrogenic properties of the particular strain of H. streptococcus and/or the sensitivity of the subject to this toxin?*

**A.**—The knowledge that the same streptococcus may cause scarlet fever in one member of a family or community and sore throat without rash in another is not more than 15–20 years old, but already health authorities are recognizing that it is illogical to isolate the case of scarlet fever and not the case of tonsillitis due to the same streptococcus. Thus the notification and hospital isolation of scarlet fever are rapidly declining, and wards for scarlet fever are now almost as rare as wards for diphtheria in many infectious diseases hospitals. The present mild nature of scarlet fever and the increasing use of penicillin therapy have helped to encourage the home nursing of this illness, and the public is losing its fear of the fever that claimed many thousands of victims in the latter part of the nineteenth century. Legislative changes must always lag behind advances in knowledge, and, of course, it is possible that scarlet fever may again become a severe infection, requiring hospital care. It may be added that in semi-closed communities, such as day and residential schools, the early notification and isolation of the first case of scarlet fever may help to prevent the spread of streptococcal infection through the community.

### Flaking on the Face

**Q.**—*What is the best treatment for flaking above the eyelids, around the nostrils, and in the nasolabial folds which does not respond to emollient creams? There is dandruff of the scalp, but it is not excessive and is improving.*

**A.**—This is presumably a mild degree of seborrhoeic dermatitis, so that treatment of the dandruff in the scalp is important. The lesions on the face will probably respond to a cream such as unguentum aquosum *B.P.* with the addition of 1% of salicylic acid and 1% of sulphur. The condition is liable to recur, but an occasional application of this cream will probably cut short recurrences. The use of soap and water for washing is not harmful, but the skin of the face is sometimes very sensitive in these patients, and one should be on the look-out for sensitivity to cosmetics and other external contacts.

### Treatment of Dandruff

**Q.**—*What is the best treatment for dandruff? A woman with very thick hair has had this condition for 16 years, and complains of scaliness of the scalp and at times intense itching. Applications of spirit lotions give only temporary relief. Would cutting her hair short have any effect on the condition?*

**A.**—There is no permanent cure for dandruff. It is usually possible to keep the scalp clear with regular treatment, but the dandruff will recur within a few days or weeks if treatment is stopped. Cutting the hair short is not likely to make much difference except that it may make the application of creams and lotions easier to carry out.

For dandruff of a severe degree cream is usually best. A suitable base is an emulsion of:

| | | |
|---|---|---|
| Liquid paraffin ... ... ... | 12½ | parts |
| Emulsifying wax ... ... ... | 5 | „ |
| Rose water ... ... ... ... | to 100 | „ |

Into this base may be incorporated 1 or 2% each of salicylic acid and sulphur.

The cream is reasonably pleasant to use and is not excessively greasy. The scalp should be washed with soap and water once or twice a week.

Once the dandruff has been brought under good control a lotion such as the following may be applied twice a day:

| | | |
|---|---|---|
| Chloral hydrate ... ... ... | 2 | parts |
| Salicylic acid ... ... ... | 3 | „ |
| Castor oil ... ... ... ... | 4 | „ |
| Spirit ... ... ... ... | to 100 | „ |

The use of this lotion, perhaps with occasional application of the cream, should continue indefinitely.

### Polycystic Kidneys

**Q.**—*A father, aged 38 years, with two children aged 12 and 4 years, has bilateral polycystic kidneys. There is a strong family history of the condition: his mother died of polycystic kidneys at the age of 40; two sisters, one of whom died aged 41 years, and a brother are likewise affected. What are the possibilities of the children being affected? Both are females. What is their outlook?*

**A.**—Polycystic kidneys may be due to a dominant gene, and in view of the history there can be little doubt of it in this family. The chance of the father passing on the gene to any child is therefore one in two. The chance that a child will develop symptoms is, however, considerably less, for not infrequently there are none and the condition is only discovered post mortem. It may also be that sometimes the gene is not expressed at all, and so a carrier may have normal kidneys, though in an abnormality which may only be manifest at necropsy it is obviously difficult to be sure about this or to make any estimate of chances.

### Oral Testosterone in Cancer of the Breast

**Q.**—*Testosterone propionate has been recommended for mammary carcinoma recurrences, and does appear to be of some benefit. Is methyl testosterone (the oral preparation) equally efficacious?*

**A.**—Testosterone propionate is useful in the treatment of mammary carcinoma, but is not curative. It is the hormone of choice before the menopause and whenever there are bone metastases. The effective dose is 150 mg. weekly, given in three divided doses by injection, and the treatment should continue for three months or longer. If no effective response occurs in this time there is no point in continuing. A weekly total dose of 150 mg. appears to be as effective as 300 mg.

Methyl testosterone is equally effective in adequate dosage. This has been found to be 200 mg. daily by mouth, in tablets of 50 mg. There is no great difference between swallowing and allowing to dissolve under the tongue. There is some clinical indication that the methyl testosterone should be continued for six months rather than three months as an initial course, but further experience is necessary. See also "Report of Committee on Research of Council on Pharmacy and Chemistry on Current Status of Hormone Therapy and Advanced Mammary Cancer" (*J. Amer. med. Ass.*, 1951, **146**, 471).

### Vitamin E and Vascular Disease

**Q.**—*What place has vitamin E in the treatment of intermittent claudication or angina pectoris?*

**A.**—The position of vitamin E in the treatment of both intermittent claudication and angina pectoris is still unsettled. Published work purporting to show its value has been poorly controlled, and the articles concluding that it has no value are so far not convincing. For the last two years a personal investigation on the effect of alpha-tocopherol on occlusive coronary atherosclerosis has yielded negative results. According to at least one English authority, vitamin E in doses of about 300 mg. daily helps to relieve the symptom of intermittent claudication.

### Advice for the Mother of an Anencephalic Monster

**Q.**—*A married woman, aged 27, in good general health, has had four full-term pregnancies (no miscarriages) in the past eight years. The first resulted in a stillbirth (normal foetus); the second in an anencephalic with hypospadias; the third in a normal boy, who is alive and well now; and the last in another anencephalic monster with (?) hypospadias. The mother is anxious to have another child, but naturally she is very frightened at the possibility of further monsters. What advice should I give her?*

**A.**—Familial incidence is not high in anencephaly. The chance that a subsequent child will suffer from anencephaly after one anencephalic monster has been born is about 1 in 40. But just because the familial incidence is low it is difficult to say what are the chances after two anencephalic monsters. It may be that the chance is increased; we do not know, but it is unlikely that the risk is more than a small one. It is unlikely to be greater than, say, 1 in 20, and, bearing in mind the risks inherent in any pregnancy, there seems to be no sufficient reason for dissuading this couple from having another child.

### Therapeutic Abortion and the Law

**Q.**—*What is the present state of the law on the termination of pregnancy? Have recent High Court rulings broadened the narrow range of indications allowed?*

**A.**—The law does not specifically recognize that termination of pregnancy is ever lawful, but it implies that it can be, and it has long been accepted that abortion may be induced if continuation of pregnancy threatens the life of the mother. The case of Rex *v.* Bourne (1938) clarified the interpretation of the law in so far as it made it no longer necessary to show that the life of the mother is *immediately* threatened by the pregnancy. The judge in this case directed the jury that if a doctor believed that pregnancy would make the mother a "physical or nervous wreck" he could be regarded as operating to preserve her life. More recently, in Rex *v.* Bergman and Ferguson (1948), this view was confirmed, and the judge further pointed out that, provided the doctor's opinion about the threat to health and life was an honest one, it need not necessarily be a correct one.

The exact indications for therapeutic abortion are therefore still not defined by law, and every case requires to be judged on its merits. To justify abortion it must be honestly believed that continuation of pregnancy seriously threatens the physical or nervous health of the woman, and even then it is unwise to interfere without first having a second opinion from a medical colleague of high repute.

### Are there Hormones in Breast Milk?

**Q.**—*Are hormones, in particular oestrogens, excreted in human milk?*

**A.**—No.

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON, W.C.1. TELEPHONE: EUSTON 4499. TELEGRAMS: *Aitiology, Westcent, London.* ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.
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